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ON RETINITIS PIGMENTOSA AND ALLIED DISEASES.

By E. Nettleship.

The diseases noticed in the present paper are retinitis pigmentosa (including the so-called retinitis pigmentosa sine pigmento), retinitis punctata albescens (Mooren and Gayet), atrophia gyrata choroideæ et retinæ (Fuchs), and congenital stationary night-blindness without changes. Whether the last-named disease is of the same essential nature as retinitis pigmentosa or not, the two conditions are so much alike in their symptoms and natural history that they may conveniently be considered side by side.

My principal object has been to appraise the share taken by heredity and consanguinity in causing these maladies, and especially to ask whether blood-relationship carries any influence at all, apart from the existence of a predisposition to the disease in the two consanguineous parents or ancestors. I have, therefore, analysed all the published cases I could get access to, adding my own (about 100) and some other unpublished ones placed at my disposal by friends.* The result is a series of nearly one thousand families, containing about seventeen hundred persons affected with retinitis pigmentosa, and upwards of fifty families, containing nearly three hundred individuals affected with some one of the other three diseases. By "family" I mean

* Mr. Marcus Gunn, Mr. Lawford, Dr. E. J. Smyth, Professor La Gleyze of Buenos Ayres (through Dr. Mackenzie Davidson), and others.

genealogy or pedigree, *i.e.*, all the persons who are known to be related to one another by blood. Naturally a large proportion of the notes include only two generations, and only two or three persons—parent or parents and child or children. Such incomplete records, though of little value in regard to heredity, are useful for statistics of sex and age, or sometimes as illustrating special features of individual cases.* The series now dealt with enables us to carry the subject somewhat further than the point reached by Herrlinger, who, in 1899, collected the facts of between six and seven hundred families. In preparing the data I have cast out all cases where syphilis, either acquired or inherited, seemed probable, and thus the nett numbers that I have accepted differ in a few instances from the various published totals: the alteration of the grand total thus caused, however, is but small. When an author gives only numbers, without details of his cases, his figures have, of course, been accepted.

I hope to give some attention also to several other features of the disease in addition to heredity and consanguinity.

Although retinitis pigmentosa is a somewhat hackneyed subject, a few words of introduction may not be out of place.

The occurrence of permanent night-blindness and its liability to run in families have been known for a long time (Ovelgün, 1744; Samuel Pye; Richter, 1828; Cunier, 1838; Stiévenart, 1847); and very soon after the introduction of the ophthalmoscope the cases were separated into those in which morbid changes could be seen at the fundus, and others (a minority) in which the appearances were normal and remained so. The cases in the former class continue to be known for the most part as retinitis pigmentosa, the name which seems to have been originally given to the type by Donders; but later observations have

* The exact numbers are:—Retinitis pigmentosa, 976 families with 1,681 persons known to be affected; Retinitis punctata albescens, 11 families with 20 affected persons; Atrophia gyrata, 4 families with 10 patients (but I know of several other families probably belonging to this category); Congenital stationary night-blindness, 36 families with 260 affected members (not including Cunier's celebrated case, still under investigation, with the aid of Professor Truc of Montpellier).

led to the recognition of the two sub-groups or varieties mentioned above. In the second class, night-blindness without visible change, we find two very different groups—different species, we must suppose;—in one, the night-blindness is present from earliest childhood, *i.e.*, doubtless from birth, is permanent, does not get worse, and is very often hereditary; in the other kind the night-blindness may set in at any time of life, is temporary, curable and depends upon exhaustion of a poorly nourished retina by excessive exposure to sunlight,—the so-called functional, essential, idiopathic or acute night-blindness. Only the permanent congenital kind will be considered in the present paper.

Retinitis Pigmentosa.

Liebreich, seeking an explanation of the prevalence of retinitis pigmentosa in certain families, discovered that the subjects of the disease were often the children of cousins, and his classical paper on the subject, published in 1861 (aided, doubtless, by the illustrations of the ophthalmoscopic changes given in his incomparable Atlas, 1863), did much to stimulate enquiry as to the influence both of consanguinity and heredity in producing the malady.

Since that time the literature of retinitis pigmentosa in relation to heredity and consanguinity has become very extensive, especially on the Continent. In our own country, Hutchinson was one of the first to record cases; and Soelberg Wells, Argyll Robertson, Swanzy, Fitzgerald, Zachariah Laurence, Windsor, and others were amongst the early contributors.

No one doubts now that retinitis pigmentosa is often hereditary. There is not quite the same unanimity of opinion as to the frequency of blood-relationship between the parents or earlier ancestors of those who suffer; whilst amongst those, and they are the great majority, who maintain or allow that consanguinity often occurs, different views are taken as to its significance and importance in relation to the disease. Authors who base their opinions on

these points upon personal experience alone are not likely to agree, because in a number of small series of cases the proportion of each series in which either heredity or consanguinity is recorded will be found to vary within wide limits. Such discrepancies are due in part to accident, but chiefly to the quality of the note-taking, the knowledge or communicativeness of the patients, and to the cases being or not being selected, consciously or otherwise, by the observer; thus in my own series the hospital cases show much less consanguinity than the private ones, though in regard to heredity there is not much difference. Occasionally the note "no history of consanguinity" may have another explanation than the patient's ignorance: a colleague of mine, asking the father of a batch of retinitis pigmentosa children whether he and his wife were cousins, got for answer "No, sir," but the man then called him aside and said, "You know, sir, we are uncle and niece." In fact, examination of a sufficiently large number of cases proves beyond the possibility of doubt that the victims of this disease are very frequently the children of blood-relations; the relation is usually that of first cousinship, but it may be more remote and is occasionally much nearer. The following general statement shows approximately the position as regards heredity and consanguinity at the present time.

In the 976 families mentioned in the footnote to p. 2, I find evidence of heredity without consanguinity in 230, or 23·5 per cent., of consanguinity without heredity in 226, or 23 per cent., and of heredity combined with consanguinity in 32, or between 3 and 4 per cent. These 3 items make 488, or exactly one-half of the total 976. Thus in half of the recorded cases the available notes give no information about these two factors, a proportion that would, of course, have been very much reduced and the proportion of hereditary and consanguineous cases correspondingly increased had the investigations been more thorough; it is, indeed, not unlikely that if the enquiry could always be exhaustive, the number in which there was neither heredity or consan-

guinity would be brought down to a very low figure. At any rate if we look only at the 488 families in which one or other of the two factors we are considering was found, it appears that heredity and consanguinity were present in virtually equal proportions.

Both heredity and consanguinity are found in several degrees and various modes, and I propose to illustrate some of these differences rather fully, perhaps tediously, by diagrams of pedigrees. Hereditary cases will be taken first, for the significance of consanguinity cannot be gauged until the facts of inheritance have been considered.

The simple terms heredity, inheritance, and transmission are not always explicit enough. Qualifying words are needed to define some of the different modes of transmission, and I propose the following :—

1. Continuous direct inheritance: Inheritance by child from parent (or transmission from parent to child). It is sometimes convenient to speak of continuous indirect inheritance when an uncle or aunt is affected but not the parent.

2. Discontinuous or indirect inheritance: All cases in which the disease disappears for one generation or more, crops out in an earlier generation (atavism), or affects uncles or aunts of the patient but not parents, or cousins of the patient but neither parents nor uncles or aunts. ("Indirect" or "Latent" heredity of Bollinger.)

3. Collateral or lateral: Affection of brothers and sisters (siblings) only: I count these cases as showing heredity, because it is doubtful whether retinitis pigmentosa has ever arisen *de novo* when it affects several members of a childship.

4. Double or reinforced: When the disease is derived from or through both parents. ("Potenzierter" heredity of Bollinger.)

5. When there is reason to believe that heredity or transmission shows itself under different guise in the various generations or individuals of a family (*e.g.*, retinitis pigmentosa alternating with deaf-mutism, etc.), the term "Dissimilar" or "Equivalent" inheritance is appropriate

("Ungleichartig" or "variiert" Bollinger), "similar" ("gleichartig") inheritance being ordinary inheritance or transmission of the same disease.

KEY TO THE SIGNS USED IN THE DIAGRAMS.

♂, *Male.* ♂, *Male affected with retinitis pigmentosa.*

♀ or ♀, *Female.* ● or ●, *Female affected with retinitis pigmentosa.*

○ or ●, *Sex not stated*, affected or not according to sign.

◯, *Several siblings or sibs unaffected;* a number within the circle shows how many. If all are of same sex, the corresponding sign is added.

Siblings or sibs, brothers and sisters.

⊖ or ⊗, *Male or female affected with deaf-mutism, idiocy, or some other congenital degeneracy considered as equivalent to retinitis pigmentosa.*

Childship, the children of any one pair.

Parents joined by a bracket above, ♀ ♂, are cousins; degree of cousinship sometimes indicated by "1st," "2nd," etc., above bracket.

Twins are joined by a horizontal line, ♂—♀.

A wavy line (~) *beneath a childship* means that the order of birth is not known.

Successive generations are indicated by Roman numerals at the side.

Heredity.

As already stated, heredity alone, either continuous, discontinuous, or collateral, without consanguinity, was found in 230 families, rather more than 23 per cent. of the entire series or 47 per cent. of the 488 families in which either heredity or consanguinity was proved. Continuous inheritance is illustrated in the following cases with Figs. 1 to 14.

Of extensive pedigrees properly worked out I know of only two. One of these families, now recorded for the first time and illustrated in Fig. 1, has been under my own notice since 1883;* the other was published by Snell in 1903

* I have satisfied myself that the family mentioned, but not described in detail, by Hutchinson, in the Medical Mirror, 1869, September 1, and again in the Ophthalmic Review, vol. i, p. 2 (1882), is the same as the one I now record. Mr. Hutchinson's patient was Generation IV, No. 1, in my Fig. 1.

(Fig. 2). Several examples are mentioned by authors in which the disease had been known in the family for from one to two centuries (Wider, Cases 13 and 25, Kerschbaumer, Cheatham's case given by Webster, a case mentioned by Hansell and another by Harlan),* and though, unfortunately, the full particulars are not given in any of these, such fragmentary records have their use as proving that a persistently hereditary character is not very infrequent in this disease.

Case 1.—In my case of seven generations (Fig. 1) 38 persons are or have been affected with retinitis pigmentosa in a total of 200, nearly 1 in every 5; the sexes were practically equal both in the healthy and diseased, the males being very slightly in excess in both (the numbers are given on the diagram, Fig. 1). The number of childships was 40, varying from 1 (in 4 instances) to 11 and 12. In regard to the relative fertility of the affected and normal; of 12 affected males in Generations I to V,† 7 married and all had children amounting to 25 ($3\frac{1}{2}$ each), against 4 unaffected with 22 children ($5\frac{1}{2}$ each); of 14 affected females all married and had children, amounting in all to 69 (5 each) against 13 healthy ones who are known to have married and had 81 children (6 each).‡ The average issue of each marriage of a diseased parent was, therefore, decidedly, though not very much, less than the average for each marriage of healthy parents—as $4\frac{1}{2}$ to 6. It by no means follows that these figures point to lessened fertility; there are probably other and simpler reasons. There is no instance of marriage between an affected man and woman, but in two cases an affected woman married a healthy cousin from within the affected branch of the family, and in each of these exactly half of the children were affected; the same proportion, however, is observed in more than one of the childships in which the parents were not consanguineous.

* Both Dr. Cheatham and Dr. Harlan write that they are unable to supplement their published accounts.—E. N., November, 1906.

† Generations VI (with one exception) and VII are too young to have children, or are unmarried.

‡ It is uncertain how many of the remaining 17 normal women and 23 normal men married.

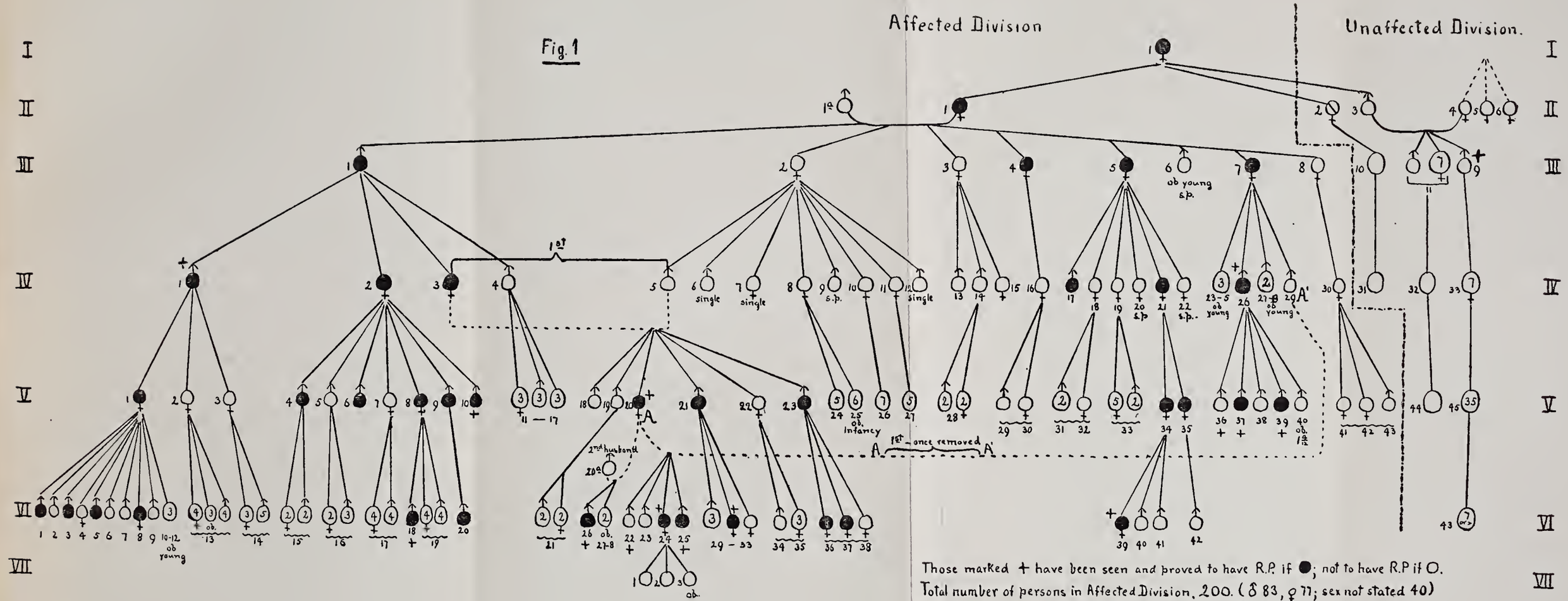
Descent of the disease in this family was invariably continuous no healthy pair ever having an affected child.

The disease was transmitted by the father 6 times and by the mother 11 times.

Not a single case of deaf-mutism, mental defect, or other degeneracy has occurred in this genealogy. The members have been occupied in various small trades or as artisans, and the ones I have seen were above the average of their class in intelligence. They are decidedly long lived.

The now living head of the family, George Young, Generation IV, 26, aged 66 (in 1905), has been blind of retinitis pigmentosa for many years. He is a Hampshire man: his wife was from Warwickshire. I saw him first in 1883 and 1884, when he was 44; the R. had then been blind for three years, and presented a complete over-ripe cataract; the L. fundus was visible in spite of posterior cortical cataract, and showed extreme retinitis pigmentosa, and there was still a little sight in this eye. He said he could not remember ever having seen well at night, and believed his day vision had never been so good as that of other people; but he could see to go about easily by daylight till he was about thirty-six. He was the fourth born of seven children, and only one other, the seventh (IV, 29), lived to grow up, had good sight, and died, æt. 36, of typhoid fever. Nos. 1, 2, and 3, sexes unknown, and Nos. 27 and 28, boys, all died in infancy, and it is very probable that some of them would have been affected by the disease if they had lived. He has had five children, all sons (V, 36—40); the youngest (V, 40) died æt. 16 months, the other four were (and are still, 1906) living; two of them are normal, two (Arthur and Henry) have the family disease. He brought the two latter for advice in 1883. Alfred (V, 37), at that date æt. 11, had in each eye My. 6 D, and V, corrected 20/70 and read 1 J; fair complexion, hair straw-coloured: no retinal pigmentation visible by indirect examination, but by direct method at periphery a few grains of pigment in retina, and pigment along one or two retinal veins: haze of retina at periphery, and choroid at same part dappled with palish spots; slight loss of upper part of each F. In October, 1905 (æt. 32) I saw him again: hair now nearly black, irides brown, very abundant retinitis pigmentosa and posterior polar cataracts.

Fig. 1



Those marked + have been seen and proved to have R.P. if ●; not to have R.P if ○.
Total number of persons in Affected Division, 200. (♂ 83, ♀ 77; sex not stated 40)
" " " " with Retinitis Pigmentosa, 38 (♂ 20; ♀ 18)

Henry (V, 39) was aged five when first seen in 1884 with V, 20/100, improved to 20/70 by −1 D., and read 1 J at 6″, media and o. ds. n., choroid at equator showed round pale dots; some dots and lines of pigment in retina at inner periphery; a patch of complete atrophy of choroid at outer periphery of R. October, 1905, æt. 26, media clear, typical and abundant retinitis pigmentosa in both eyes: can still read and write, but not easily.

At the same date (October, 1905) I also examined the eldest (V, 36), æt. 34, and found him normal; the other normal living brother (V, 38), æt. 28, was abroad: Nos. 36 and 38 have married lately, but at present have no children; Nos. 37 and 39 are single. Their mother, æt. about 65, told me that she used to know which of her children were affected almost when they were in arms, and that by the time they were about four years old the defect was evident enough; she considered that the youngest (V, 40), who died æt. 16 months, was unaffected.

The others of this genealogy that I have examined are:—V, 20, and four of her five living children (VI, 22 to 26) all characteristically affected in different degrees; 26 is the slightest case, æt. 17; 24 has been night-blind all her life; 25 has severe changes and has been night-blind as long as she can remember, now æt. 22:—VI, 18, æt. 14, who has dappling of choroid at periphery, slight typical pigmentation of retina and shrunken arteries, and cannot remember ever having seen well at night:—V, 10, æt. 35, with advanced typical changes; he had just married (October, 1905):—VI, 29, and the three children of V, 34, of whom the eldest, æt. 20, has advanced changes and much loss of F., but can still read and sew well, and has about 9 D. of My:—VI, 26, æt. 17½, shows decided shrinking of retinal arteries and waxy haze of o. ds., and is distinctly night-blind according to the testimony of his friends, though he himself is reluctant to admit it. Note that this lad, VI, 26, slightly affected, is the issue of his mother's second marriage, the husband not being her cousin and she being about 36 when she married him; whilst Nos. 24 and 25 by her first husband, who was her cousin and of the affected stock, are both badly affected, and have been night-blind as long as they can remember. V, 20, was aged about twenty-five when VI, 24, was born. IV, 1, was, as has been mentioned

above, seen by Mr. Hutchinson at the age of 49, in 1869; he had been failing from boyhood, but could then still read large letters and see to do his work; he died at 86, in 1903.

My information has been obtained from George Young (IV, 26), and agrees with the less detailed account given by Mr. Hutchinson* of IV, 1. He (IV, 26) knows that his mother (III, 7, who died æt. 70, in 1876, having been blind for 20 years), and two of her sisters and her brother (III, 1, 4, 5) were all night-blind and became quite blind; he also knew his cousin IV, 1, already mentioned. From these sources he (IV, 26) learnt further that his mother's mother (II, 1), and her mother (I, 1), had the same complaint. III, 1, who was a local preacher in the Isle of Wight, lived to be 90, and died about the year 1876.

I have also been able to see and examine the eyes of III, 9 (James White), the youngest of nine, now aged 90 (1906), hale and active, and with perfect eyes, a nephew by his father (II, 3) of II, 1. His father (II, 3) had good sight so far as is known; he was a pilot, and was drowned when he was 50, about the year 1817. III, 9 gave me the particulars of II, 2 and 3 and their descendants, including himself and his descendants, as shown in Fig. 1, from which it appears that no blindness is known in these portions of the stock; II, 2, who died æt. 70, about 1836, was blind for some years before her death, but had good sight until she was well advanced in years.

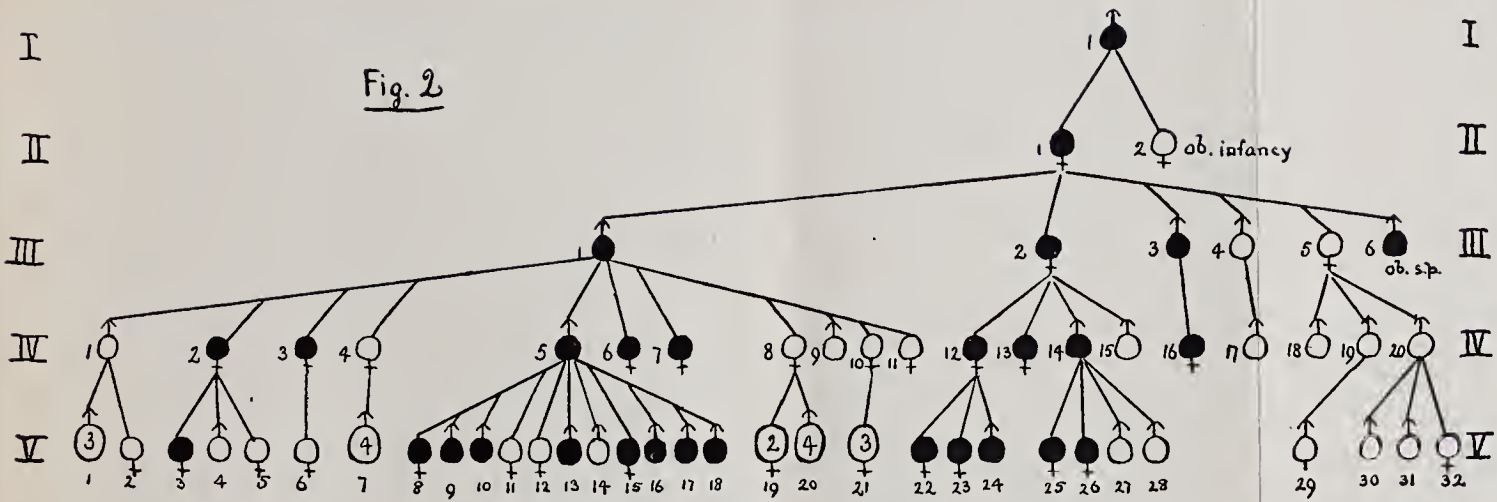
III, 8, who had only one child, died at 40, in 1855. The sibs, IV, 17 to 22, all grew up and married. Those of IV, 5 to 12, also all grew up, and their history is well known to my informant, and none are affected. V, 11 to 17, consisted of nine children, of whom the six eldest (Nos. 11 to 16) grew up and had good sight, the three youngest (represented by No. 17) died in infancy; they were born between about 1855 and 1875; I have no entry of their children, but it is known that none are affected.

Case 2.—Snell's case, of *five generations* (Fig. 2), shows 29 persons affected in a total of 72, about 1 in every $2\frac{1}{5}$. It contains 14 complete childships, varying in number from one (in four instances) to 11 (two instances). The total number of males was rather greater than the total of females, but the proportions

* Hutchinson, *loc. cit.*

(*To face p.* 10.)

Fig. 2



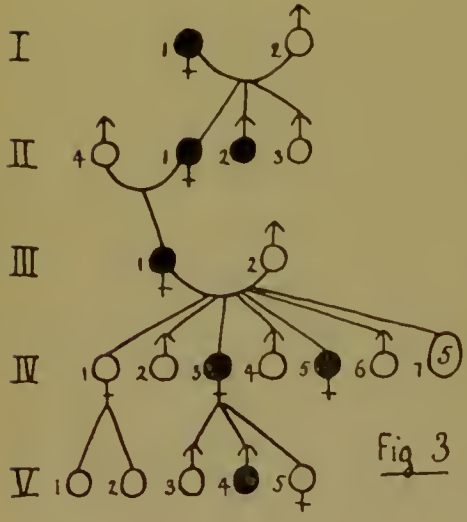
Total number of persons . . . . . 73. (♂ 39; ♀ 34)

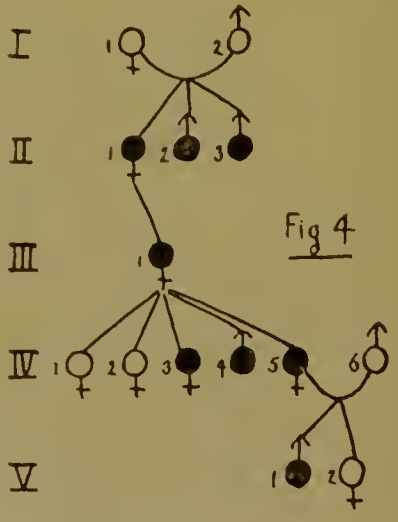
" " " " with Retinitis Pigmentosa 29. (♂ 13; ♀ 16)

of males to females in the members with retinitis pigmentosa was reversed. The disease did not interfere with fertility, 10 pairs, in each of which one parent was affected, producing 41 children, whilst eight healthy pairs had 35 children. Those males who married in Generations I to IV* (5 out of 6) had nearly 6 children each, whilst the normal males who married (only 4 out of 8) had only $2\frac{1}{2}$ children each; but no such marked difference was observed in the number of children born per head by the affected and unaffected women (5 out of 9 affected women married and had 13 children, rather less than 3 each; 4 out of 5 normal women had 16, or 4 each). The inheritance was continuous in every instance, no normal pair ever having diseased offspring. There appear to have been no cases of deaf-mutism; indeed, no degeneracy except that of the retina. The symptoms began in childhood in all the cases. There was not a single consanguineous marriage.

* Generation V consisted chiefly of children.

Case 3.—The next best pedigree (Fig. 3) showing continuous inheritance through five generations, is given by Schneider (p. 31); it would have been complete if we could be certain (as is probably the case) that III, 1 was an only child. Here, again, the retinitis pigmentosa seems to have been the only form of degeneracy in the family. I, 1 was "born blind," died in 1852 æt. 72 and had 3 children (II, 1, 2, 3), of whom No. 1 was night-blind from youth, totally blind æt. 40, and died at 65; No. 2 was "born blind," and died æt. 2; No. 3 became blind "from cold," æt. 5, and died æt. 7. III, 1 appears to have been an only child; she bore 11 children (IV), of whom one (No. 6) died with good sight æt. 8, and five others (No. 7) at about 1½ year; five lived, of whom IV, 3 is affected and has three children, one of which (V, 4) is affected; IV, 5, affected, is unmarried; IV, 1, 2, 4 normal, and No. 1 has two children reported normal.

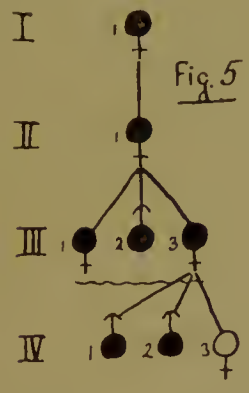


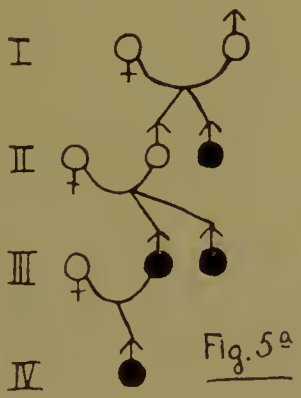


A pedigree of the disease in *four generations* is given by Ayres (Fig. 4). No information about Generation I. All the three known members of Generation II were blind, probably from retinitis pigmentosa. The only known member of III was blind, probably of the same disease, and lived to be 89; of her five children (IV) three had the disease, and the only one of these

that married passed it down to one of her two children (V, 1). No mention of any other family degeneracies.

Leber also gives a case with four generations complete as to Generations III and IV (Fig. 5). He states that III, 3, the mother of IV, 1, 2, 3, had the disease only in a slight degree. It was one of her sons (IV, 2) whom he saw with the disease at the age of 27.





The following show the disease in *three successive generations* :—

Fig. 5*a*, from Hocquard's Case 2.—Generation II, Nos. 1 and 2, two brothers, of whom No. 2 had retinitis pigmentosa and was living at 70. II, 1 had two sons (III, 1 and 2), affected, and aged 47 and 50 when seen; and of these No. 1 had a son affected, aged 21 (IV, 1).

Fig. 6, my own case.—John Mills, æt. 57, and his sister, æt. 70; both had the disease, as had his mother and mother's mother. He probably had more than one sibling. He had 10 children, of whom 4 died in infancy, 1 male (marked 6 in Generation IV), an idiot, died æt. 18, and 5 are living and normal. It is, of course, impossible to say whether the 4 who died young would have shown the disease.

Fig. 6*a* (Wm. Franklin, St. Thomas' Hospital, 1882); 2 out of 3 diseased in Generation II, and 4 of 7 in Generation III. In Generation IV, consisting of about 20 children in 5 childships, only 3 cases (8, 10, and 13) were known at date (1882); but as only 3 of the remainder were examined, 2 were dead and at least 2 others were less than 2 years old, other cases may have

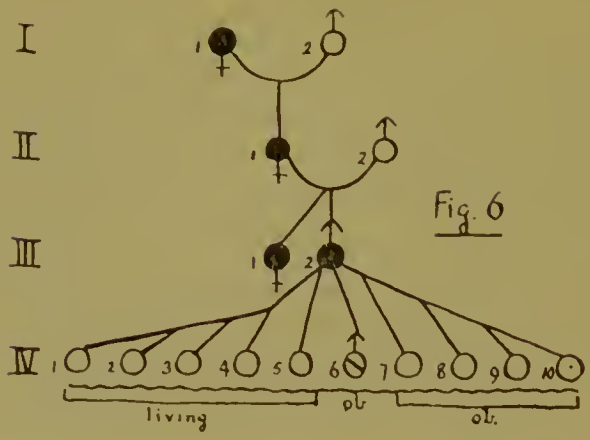


Fig. 6

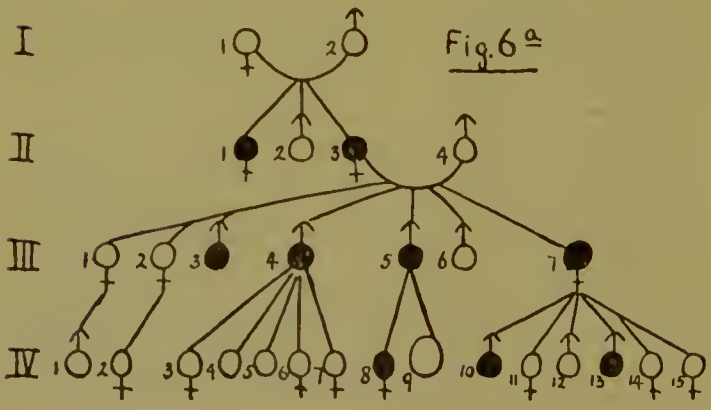


Fig. 6a

arisen at a subsequent date. No evidence of "anticipation," for it was clear from the history that the disease set in very early in life in Generation III, as well as in Generation IV.

Fig. 7, from Mooren (4, 1874), needs no explanation, except

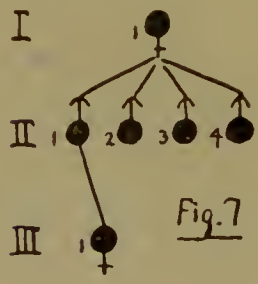


Fig. 7

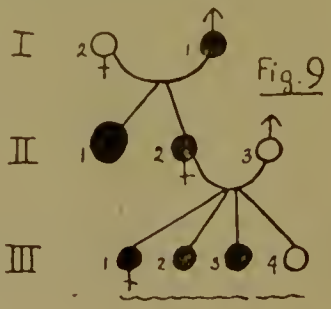


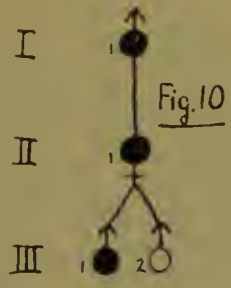
Fig. 9

that the author does not give the unaffected persons; III, 1 was æt. 19.

A case by Rosenbaum (his Case 2), is similarly incomplete, and needs no illustration.

Fig. 9 shows Case 13 of the same author. III, 1 was æt. 19.

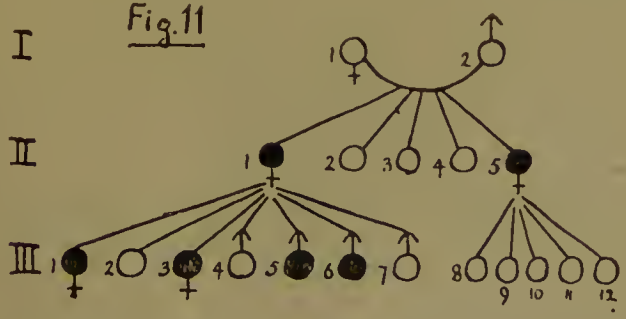
Fig. 10, from W. D. Lee (his family IV); I, 1 had retinitis pigmentosa, and became blind at 35; II, 1 had the disease complicated with cataract, and of her only two children the elder, a well-developed boy of 13, had the typical retinal disease.



Of families showing the disease, in only *two continuous generations* many examples could be given, but the following will suffice to illustrate some different modes of this degree of inheritance.

Association of Retinitis Pigmentosa and Myopia.

Fig. 11, from Ransohoff.—Inquiry showed that no cases were known in the stock before Generation II, nor had there



been consanguineous marriages. In II, Nos. 1 and 5 had retinitis pigmentosa and myopia; Nos. 2, 3, and 4 normal. II, 1,

æt. 55, had 7 children (III, 1 to 7), of whom Nos. 1, 3, 5, and 6 had the same two morbid conditions as the mother, the myopia being 9 D., 5 D., and 10 D. respectively; Nos. 2, 4, and 7 had neither retinitis pigmentosa nor myopia. II, 5 had 5 children (III, 8 to 12), 2 of whom had My. 6 D. and 9 D. respectively, but none had retinal disease.

Fig. 12 represents all that could be found out respecting the ancestry in my case of Clara Keast (Moorfields, vol. III, 5), æt. 26 (Generation III, 5), of Cornish extraction. All her sisters,

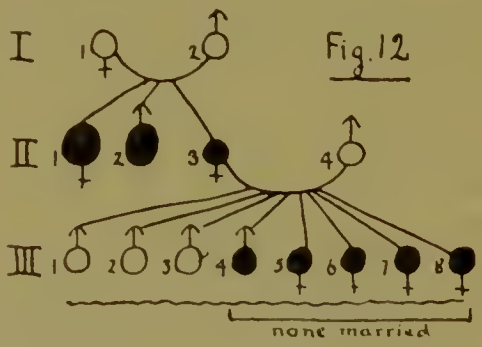


Fig. 12

1 of her 4 brothers, her mother, and several (she said "all") relatives on her mother's side had had the disease. It can hardly be doubted that we have here a fragment of a much larger pedigree, with numerous cases in several generations.

Fig. 13, Maes, "Family B" (1861).—No known ancestral cases; 2 affected in the completed childship II, 1 to 6, and 2 in

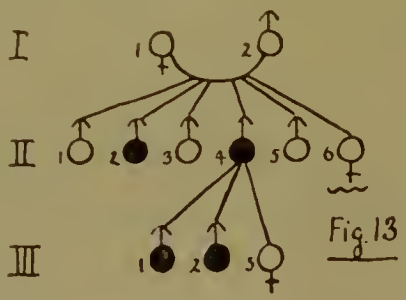


Fig. 13

the perhaps incomplete childship III, 1 to 3, the issue of II, 4. II, 4 (father) was 43, and his eldest son (III, 1) 17.

Fig. 14, my own case (Mrs. Norwood).—Generation I, a husband (1), who died of phthisis, æt. 30, and his wife (2), an only child, who committed suicide, also at 30, from grief at her husband's death ; both had perfect eyes. Of their three children one (II, 1) died at the age of 3, one (No. 2) was living and well, and one (No. 3) partially deaf, had, when I saw her, æt. 71,

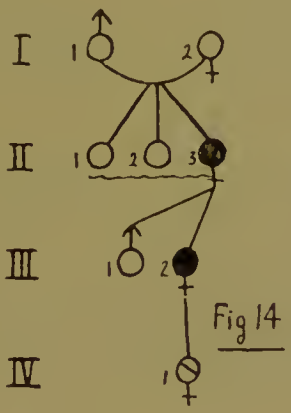


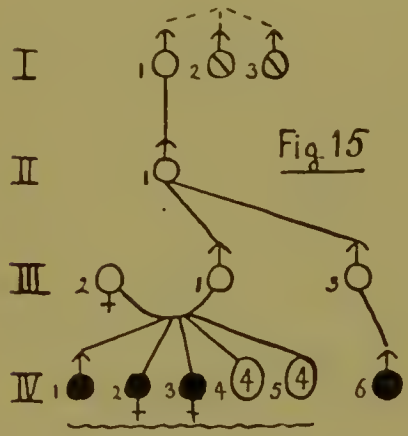
Fig 14

advanced retinitis pigmentosa and partial cataract. This one (II, 3) had 2 children only, one of them affected (III, 2), and æt. 45 at same date. She (III, 2) had only one child (IV, 1), æt. 17, *with posterior cortical cataract, but no retinitis pigmentosa.* The family history was well known for two generations above Generation II, and neither ancestors nor laterals had suffered *Note the* (*? choroidal*) *cataract in IV.*

In the cases illustrated by Figs. 15 to 22, the transmission or *inheritance was discontinuous.*

Fig. 15 (Herrlinger's Cases 22, 23) shows a deaf mute (2), an idiot (3), and a normal (1) in Generation I, but no known retinitis pigmentosa. Generations II and III, 1, 2, and 3, were all normal. In IV, in a childship of 11, 4 died young, 4 are normal, and 3 idiots with advanced retinitis pigmentosa ; No. 1 is also partly deaf, has 6 toes on each foot, and 6 fingers on the L. hand, and No. 3 has also 6 toes on each foot. A paternal first cousin (IV, 6) is deaf-mute and blind. These are all descended from I, 1, who was normal ; not only is the inheritance discontinuous for two generations, but also "dissimilar" or

"equivalent," deaf-mutism and idiocy in I, 2, and 3 being the first known degeneracy. If I, 2 and 3, and IV, 6, had not been included in the history (and such omission might easily have occurred) the case could have been claimed as showing the absence of heredity.



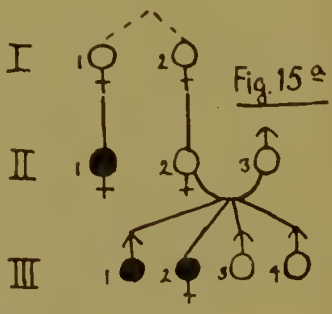


Fig. 15*a* (Herrlinger's Case 90).—Discontinuity for at least two generations in the direct line, but an aunt affected.

Fig. 15*b*, my case of Silas Pearce (St. Thomas' Hospital), is similar to Fig. 15*a*, but the affected ascendant is an uncle.

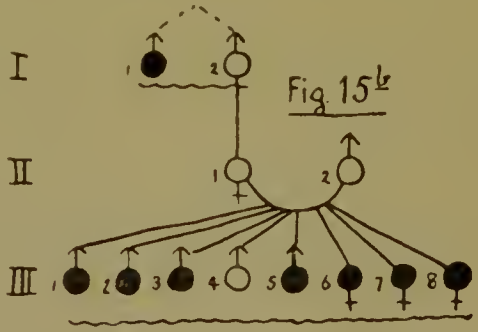


Fig. 16 (Herrlinger's Case 18).—Discontinuity for two generations; and here (as in Fig. 15) if Generation I, No. 2 had been omitted, no evidence of heredity would have appeared.

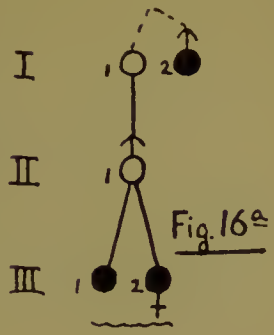
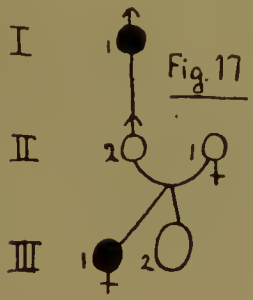


Fig. 16*a* (Siegheim's Case 17) resembles the last except as to the details of Generation III.

In the following cases the disease skipped only one generation :—

Fig. 17 (my case, P. 31, 1894).—I, 1, who was blind at 40, probably from retinitis pigmentosa; his son (II, 2) enjoyed good sight and had several children, of whom one, and one only, a daughter (III, 1), has the typical disease.



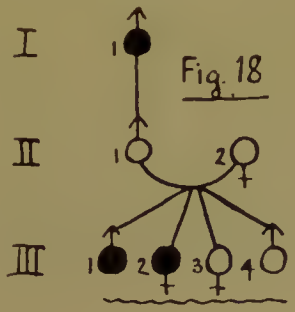


Fig. 18 (Gould).—Two siblings out of four (III, 1 and 2) affected, one (III, 4) quite normal, and in the other (III, 3) there were slight appearances of the disease, but no symptoms. Both parents normal, but paternal grandfather was night-blind all his life and went totally blind.

The same points are illustrated by Fig. 19, but with a much larger childship (Gonin's Case 11). The three affected ones (III, 2, 3, 4), were aged 20, 18 and 4.

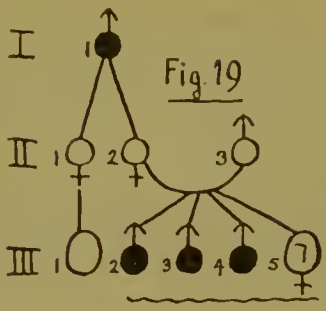
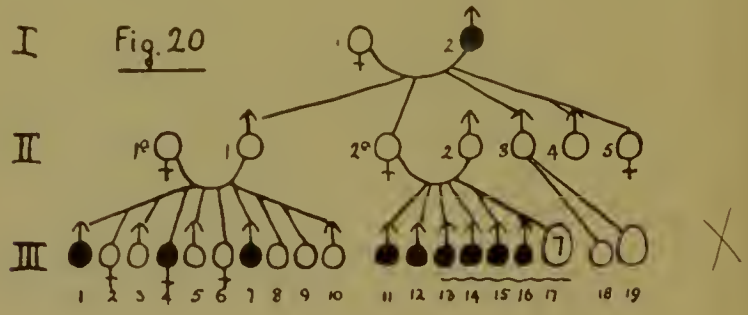
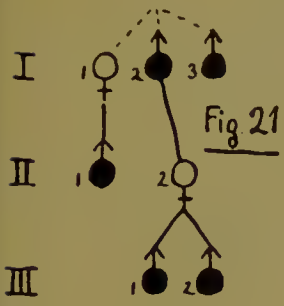


Fig. 20 (my case, Alfred Litoun) shows a much larger family with many cases in two childships. One grandfather (I, 2) is believed to have had the disease, certainly neither the wife (1, 1) nor any of the five children of I, 2, nor the wives (II, 1*a*, 2*a*) suffered. But of the 8 children of II, 1, born alive, 3 were affected, No. 1, æt. 28, No. 4, æt. 24, and No. 7, æt. 10; No. 8 was still-born and 9 died of "croup" in childhood.



II, 2*a* had 13 children (III, 11 to 17) all living when the notes were taken. I did not see any of these, but my patient (III, 1) stated that 6 of them, all males, had the disease, the other 7 (some of each sex) having good sight. Amongst those affected were the first and second born, but the order of birth of the remaining 11 is not given. II, 3 had several children, one of them "near-sighted but not like the night-blind ones," the others normal.

Seggel's Case, Fig. 21, though less simple, shows still only a single generation missed.



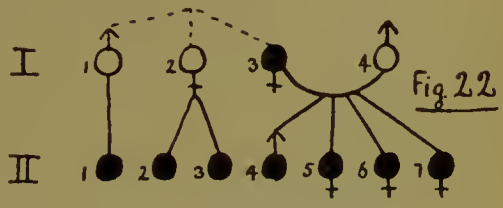


Fig. 22 (Webster's Case 7).—*Continuous and discontinuous inheritance side by side* in different parts of the same genealogy. The facts were obtained from II, 4 a man æt. 44. It is not clear whether II, 1, and II, 2, 3 were the only children of their parents.

It will be noticed that in none of the cases just illustrated (Figs. 15 to 22) does the disease skip more than two generations in the direct line, and that even then there were always side cases either of the same disease or (as in Fig. 15) an equivalent. Several other almost identical pedigrees could be given.

In the next group we have at least two, and sometimes three, generations free, indeed, no proof of inheritance at all; but in not one of these is the pedigree even approximately complete for as many as three generations.

Fig. 23 (my Moorfields case of Elizabeth Johnson, æt. 40) shows freedom from disease in the direct line for three generations above the patient (IV, 2) on the maternal and two on the paternal side; the indirect lines, however, are not known. The patient was the only one affected in a large childship, and her own four children were unaffected. She presented no signs of hereditary syphilis; acquired syphilis could not, of course, be entirely excluded, but there was nothing in favour of it and the eye changes were typical of ordinary retinitis pigmentosa.

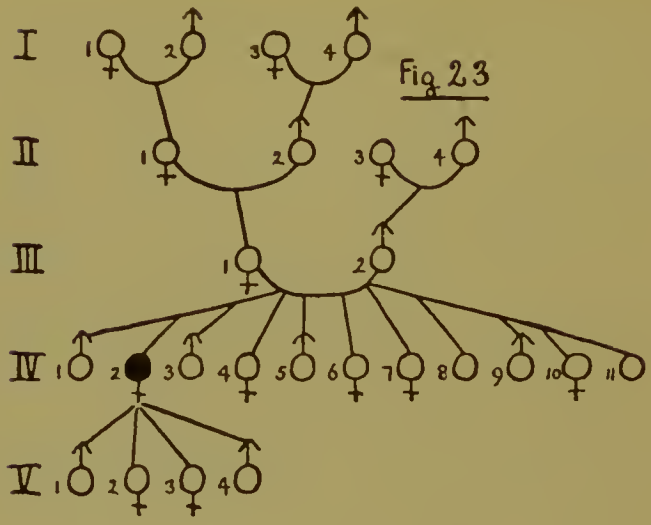
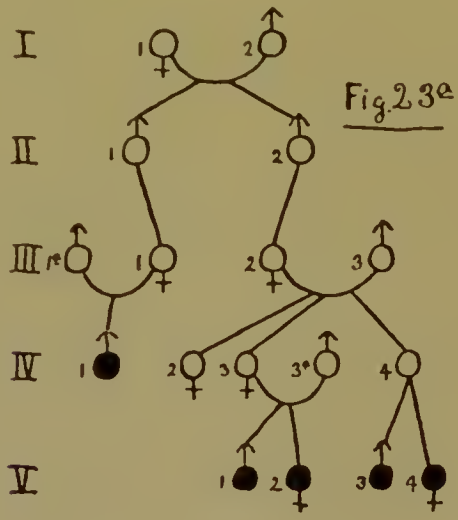
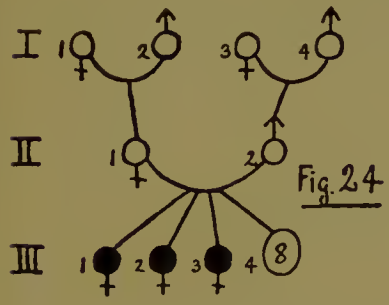


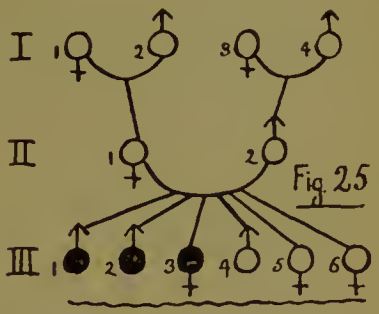
Fig. 23*a* (Neuffer, Series I, Case 6, Families B and H) is similar, but the wives in Generation II are wanting, and when the disease does appear it is more abundant. IV, 1 was aged 28; V, 1, 50; V, 2, 46 in 1879.



In the next three cases (Figs. 24, 25, 26), immunity of the four grandfathers was proved in all, and no indirect inheritance

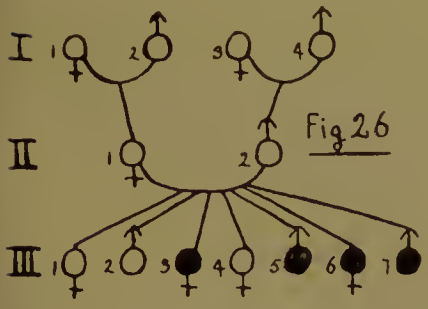
known. Fig. 24 is from Maes' (Case 16), Fig. 25 from Leber (2) (Case 4), Fig. 26 from Priestly Smith. In Fig. 24,

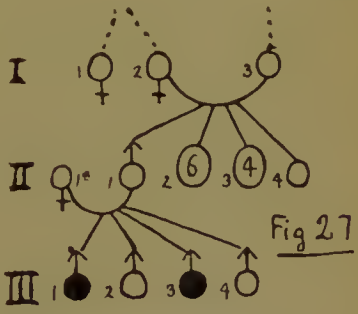




III, 1 was deaf-mute in addition to having retinitis pigmentosa. In Fig. 26 all the four with retinitis pigmentosa were also deaf, and aged between 33 and 48 when seen.

The next two pedigrees (Figs. 27 and 28) are, unfortunately, complete on one side only. In Fig. 27 (my case, P. 27, 216) the mother of the patient (II, 1*a*) was not aware of any cases in her own family, but enquiry was not exhaustive. The father

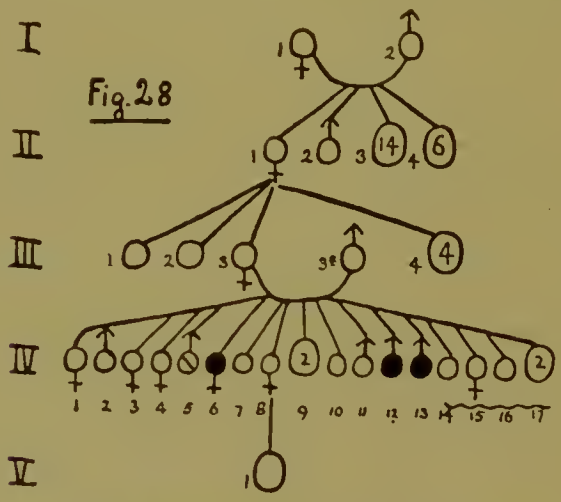




(II, 1) had had 11 brothers and sisters, of whom four died of phthisis, one of some infantile complaint, and six were living; his father (I, 3) committed suicide; his mother and her sister (I, 1, 2) died of phthisis.

Fig. 28 (my case, Moore), three cases of retinitis pigmentosa amongst 19 children born (Generation IV); 11 died young, five were living when the notes were taken (Nos. 6, 8, 11, 12, 13), but only one (IV, 8) had children and they were normal; Nos. 1 and 15 died in childbed and No. 14, at æt. 18, of an accident; Nos. 2,

3, and 4 died in infancy, No. 5, an idiot, died æt. 7, No. 6, the first of the patients with retinitis pigmentosa (æt. 40) was also deaf and half idiotic; the next with the eye disease, No. 12, æt. 30, was also mentally feeble; as to the third (No. 13), nothing is noted except the retinal disease. The mother (æt. 70)



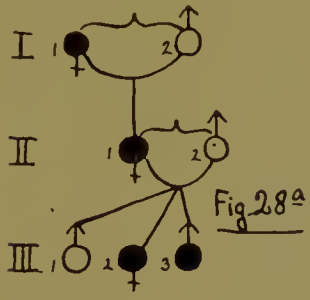
came from an old Falmouth family (Pearce); the father (Moore) (III, 3*a*) was a Devonshire man, æt. 74; his sight was excellent, but nothing was known about his ancestors. The mother (III, 3) was one of seven, three still living at date. Her mother (II, 1) was one of 22 born, of whom 15 grew up and six died young; one of the 15 (II, 2) had fits.

In the above 28 cases there was, so far as could be ascertained, no blood-relationship between the parents or earlier ascendants of any of the sufferers, except in Fig. 1, where there were two instances of cousin marriage, but in both these all the parents were members of the affected branch of the family.

In a few other families, 32 out of the total 976, both heredity and consanguinity were found and it is necessary to illustrate these. They fall naturally as regards heredity into the two groups of continuous and discontinuous descent, combined in various ways with consanguinity.

Continuous Heredity with Consanguinity, i.e., *the Parents related and one of them affected* (Figs. 28*a* to 31).

Fig. 28*a* (my case, F. Dalton, æt. 44).—Two out of three children (III, 2 æt. 44, and II, 3) have retinitis pigmentosa, No. 1, æt. 46, free, Continuous descent through two generations on mother's side (II, 1 and I, 1). Consanguinity of parents ("distant cousins") and mother's parents ("cousins"). III, 1, æt. 46, normal.



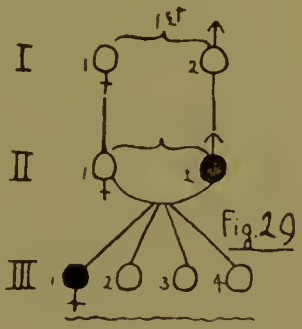
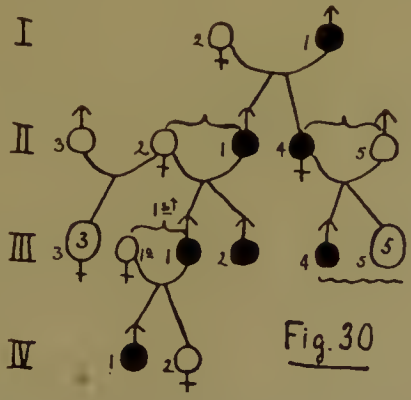


Fig. 29 (Herrlinger's Case 92), one of four siblings affected (III, 1). Direct descent from father (II, 2). Consanguinity of parents (second cousins) (II, 1 and 2), and of mother's mother and father's father (first cousins) (I, 1 and 2). III, 1, female, æt. 16.

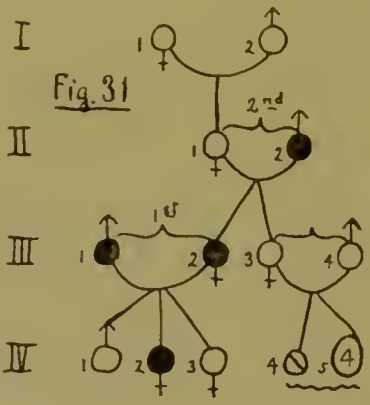
Fig. 30 (Oakley's Case 1).—Six or seven cases in five or six childships (Generation I, 1 doubtful). Continuous descent through



three or four generations. First cousinship of parents in three of the four marriages, one parent being affected in each. I, 1

believed to have been affected; II, 1 affected; first husband and first cousin of his wife (II, 2); II, 4 his affected sister, who also married a cousin; III, 1 and 2, affected sons of II, 1; III, 1, who was 46 when seen, married his first cousin (1*a*) and had two children (IV) of whom one had the disease; III, 4, one affected child out of six, issue of II, 4 and 5; III, 3, three healthy daughters, issue of marriage between the healthy parents (II, 2) and her second husband (II, 3).

Fig. 31 (Oakley's Case 2).—Retinitis pigmentosa and one case of deafness (IV, 4) in three generations; two of the patients, now dead, who had very bad sight probably from retinitis pigmentosa, were also deaf (III, 1 and 2). Continuous descent. Marriage between two first cousins (III, 1 and 2), both



of whom are said to have been deaf and had very bad sight, producing only one affected child (IV, 2, æt. 16) out of three; the other two IV, 1, æt. 22 and IV, 3, being myopic. Marriage between affected and normal second cousins (II, 1 and 2) producing one affected child out of two, the other one (III, 3) myopic.

Discontinuous heredity with consanguinity (Figs. 32 to 43).

In Fig. 32 (my case, Albert Ward, Moorfields) the descent is not only discontinuous (Generation III apparently escaping), but dissimilar, insanity in Generation II, and mental deficiency in the younger generations (IV and V) seeming to take the place of retinitis pigmentosa. IV, 1 married twice; by first wife (IV, 2), one child (V, 5) with retinitis pigmentosa, who has

two normal children (VI, 1); by second wife (IV, 3), who was his first cousin, V, 1 died æt. 6, mentally deficient, 2 miscarriage, 3, the patient, retinitis pigmentosa and deficient, æt. 13, 4, æt. 6, normal.

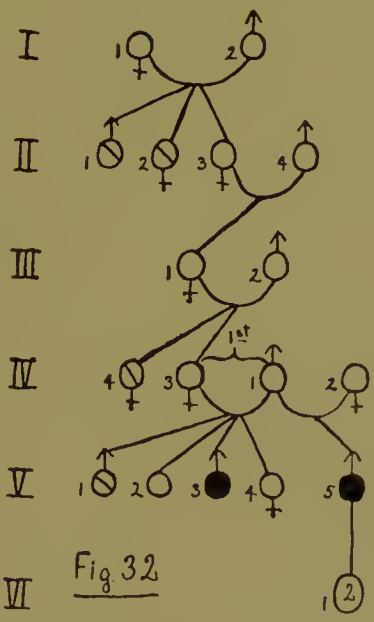
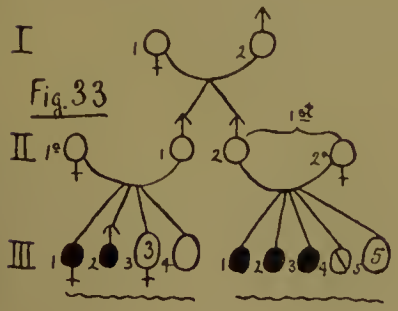
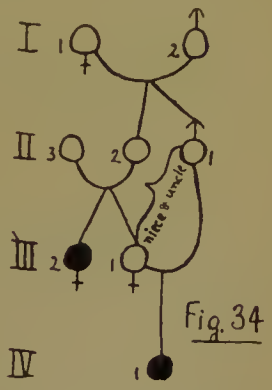


Fig. 33 (Webster's Case 4).—A healthy pair (I, 1 and 2) have two healthy sons. One (II, 2) married his first cousin (2*a*)



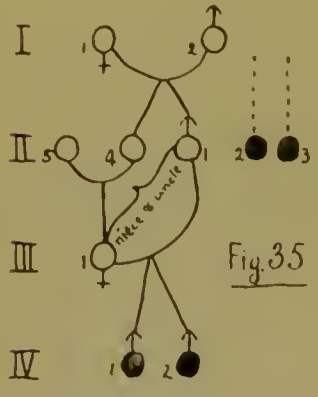


and had nine children, three of whom (1, 2 and 3) became blind and afterwards idiotic, one (No. 4) had good sight, but died of a chronic disease of the nervous system, and five were presumably

healthy. The wife (II, 1*a*) of the other brother (II, 1) was not related to him; out of his five living children, two had retinitis pigmentosa, III, 1, æt. 42, being the patient; the number who died (III, 4) is not stated.

Fig. 34 (Trousseau's Case 1), a child, aged 12 (IV, 1), with retinitis pigmentosa, was the issue of a union between uncle and niece, both normal (II, 1 and III, 1). The parents of the father, II, 1 (I, 1 and 2) were examined and found normal, but a sister (III, 2) of the patient's mother was examined and found to have retinitis pigmentosa.

Fig. 35 (La Gleyze's Case 28) is somewhat similar to the last. A healthy uncle (II, 1) marries his healthy niece (III, 1), parents and grandparents also unaffected (II, 1, 4, 5 and 1, 1 and 2). The two sons (IV, 1 and 2) of the consanguineous marriage have the disease, but it is also found that their father (II, 1) has two first cousins similarly affected (II, 2 and 3).



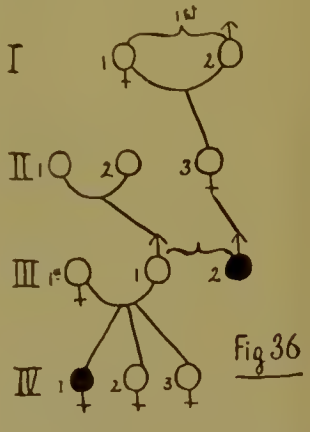


Fig. 36 (my case, P. 27, 115).—A girl of 13, with retinitis pigmentosa (IV, 1), has two healthy sisters; parents (III, 1 and 1*a*) normal and not consanguineous, but III, 2, a first cousin of the father, III, 1, became blind at 16, almost certainly from the same malady, and his maternal grandparents (I, 1 and 2) were first cousins.

Fig. 37 (La Gleyze's Case 35).—The daughter (II, 1) of healthy first cousins (I, 1 and 2) is affected; but so also is a first cousin of the patient (II, 2).

Fig. 38 (my case, P. 23, 167).—A pair of healthy first cousins (I, 1 and 2) married and had a son and daughter (II, 1 and 2), both of whom went slowly blind of "optic nerve decay" at about 45 and lived to an advanced age (one of them died at 86, the other still living at 72). II, 1 married twice and had

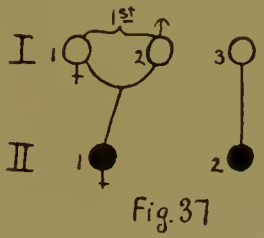


Fig. 37

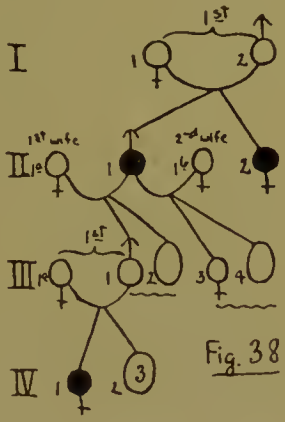


Fig. 38

healthy children by both wives; I saw and examined a daughter of the second marriage, æt. 38 (III, 3). III, 1, a son of the first marriage, aged 45 at the date of my notes, married his first cousin (III, 1*a*), and had four children, of whom the eldest (IV, 1) had seen Mr. Liebreich for night-blindness and contracted fields. The kind of first cousinship of III, and 1*a* not noted.

Fig. 39 (Neuffer's Case 26).—Two healthy first cousins have three sons (II, 1, 2 and 3) deaf-mute and blind from retinitis

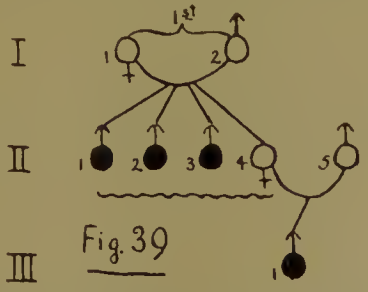
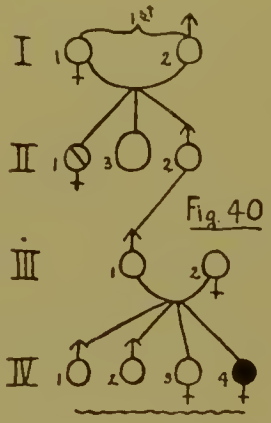


Fig. 39

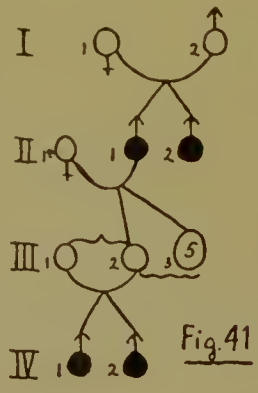
pigmentosa and one healthy daughter (II, 4). She (II, 4) married a stranger, but has a son with retinitis pigmentosa.

Fig. 40 (my Case, P. 12, 223) shows retinitis pigmentosa and deafness in one of a childship of four (IV, 4); parents, grandparents and paternal great grandparents (III, 1 and 2;



II, 2, and I, 1 and 2) all normal, but the last named (I, 1 and 2) were first cousins. A sister of the patient's paternal grandfather deaf-mute (II, 1) ("dissimilar heredity").

Fig. 41 (Herrlinger's Case 36).—Retinitis pigmentosa in two brothers (IV, 1 and 2), the sons of cousins (III, 1 and 2) them-



selves free, but one of them (III, 2) inheriting the disease from his (or her ?) father and uncle (II, 1 and 2). Parents of II, 1 and 2 normal.

Fig. 42 (Herrlinger's Case 86).—Retinitis pigmentosa in two brothers, one æt. 26 the other dead (II, 2 and 3), whose parents

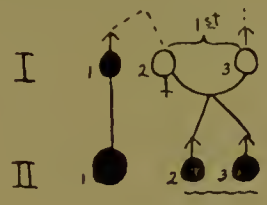


Fig 42

were first cousins. The same disease in another cousin of one of the parents (I, 1) and in several of his children (II, 1).

Fig. 43 (Derig's Cases 20 and 21).—Two men (IV, 1, æt. 21 and III, 2, æt. 43) afflicted with retinitis pigmentosa and deafness. They are double cousins, being first cousins by their fathers (II, 1 and 4) and first cousins once removed by their

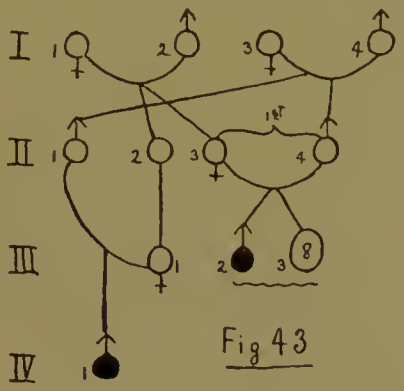


Fig 43

mothers (III, 1 and II, 3). The parents of IV, 1 (II, 1 and III, 1) were not consanguineous, but the parents (II, 3 and 4) of III, 2 and his eight healthy sibs, were first cousins. IV, 1 is preceded in the direct line by at least three normal generations.

Consanguinity.

The data for deciding whether consanguinity can produce retinitis pigmentosa *de novo*—*i.e.*, without heredity or predisposition, do not yet exist. To establish that thesis we

must be able to produce a long and complete pedigree, extending to five, six, or more generations, in which the disease was confined to a childship, or to childships, all of the same generation, the offspring of blood-relations. No such pedigree has been published so far as I know. The best known to me are included in the following diagrams, and inspection will show that not one of them satisfies the above requirements. There is not one of them that might not illustrate discontinuous inheritance (atavism), the consanguinity acting merely as an intensifying cause. We satisfy ourselves that this is so by comparing the most important consanguinity pedigrees (Figs. 45, 46, 51, 58) with corresponding ones illustrating heredity (Figs. 15 and 15*a*), and with such as Figs. 23, 23*a*, and 28, in which neither inheritance nor consanguinity appear. Since in each of these groups we find instances where three generations are free from the disease in the direct line on at least one parental side, we are not entitled to conclude that consanguinity, when it appears in such a pedigree, has originated the malady. Those authorities (and they are probably a diminishing number) who hold to the doctrine that union of blood-relations may start this disease must rely at present mainly upon its striking frequency in the issue of cousin marriages. Whether when the consanguinity is nearer than first cousinship the proportion of children affected is especially large, we have not sufficient material to decide; but if such larger proportion were proved, its significance would be important, supposing that heredity could be excluded. The only cases of such closer unions that I have found published (Figs. 60, 72, 75) do not show any preponderance of the disease in the issue, but they are too few and too incomplete to justify any conclusion.

Those who have been careful to eliminate the factor of heredity—a majority of the more recent writers—for the most part decide that consanguinity is but an expression of heredity acting through both parents, and that if both husband and wife are entirely free from taint they are no

more likely to have children with retinitis pigmentosa if they are akin by blood than if they are not. And this seems to be the position arrived at by most who have studied the subject of consanguinity in relation to other diseases or degenerations. *But it is obviously of the greatest importance, in relation to this matter, that larger genealogies of retinitis pigmentosa should be obtained.* The principal difficulty is in getting an authentic history of the *absence* of the disease in ancestors further back than two or three generations; for unless we can go back several generations, heredity, as we have already seen, cannot be excluded. In fact, the tendency to interruption or discontinuity of descent is quite a marked feature in the history of retinitis pigmentosa. This is proved, for example, in 22 families, where two affected generations were separated by a healthy one (as shown in Figs. 38, 41, etc.); and few will doubt that, had fuller search been possible, the disease would have been discovered in an earlier generation in many of the very numerous cases where the notes actually obtained state no more than that the parents, whether consanguineous or not, were themselves unaffected.

On the other hand, continuous descent from generation to generation, either from parent to child or from uncle or aunt to nephew or niece, can frequently be proved, as already shown in many of the Figures; and even when the parents were cousins, we find several instances in which one of them was affected by the disease, a fact that in those particular cases deprives the consanguinity, as such, of any value. The same conclusion as to the non-specific influence of consanguinity may be drawn from the cases that show both consanguinity and inheritance in separate branches of the same stock (Figs. 33, 34, etc.).

Again, if consanguinity were a potent cause, we should be prepared to find that the proportion of the children affected was larger in the offspring of blood-relations than of others. This, however, does not seem to be the case, for, from the available data, summarised in Table A, we

see that the average number of affected children born to each marriage was not sensibly different in the consanguineous and non-consanguineous series. It is true that the departures from the average were fewer in number and less extreme in degree in the former than in the latter; but the numbers are too small for finality.

It is therefore certain that heredity is a potent cause of retinitis pigmentosa, and that the descent, though sometimes continuous from generation to generation, either directly from parent to child or indirectly from uncle or aunt to nephew or niece,* often shows itself intermittently, and may lie hidden for as many as three (? four) generations (Figs. 23*a*, 28, 43). But of parental consanguinity we cannot at present affirm more than that it often precedes the appearance of the disease; and although we are not yet able to disprove its specific influence, all the indirect evidence at our disposal points to marriage of blood-relations being harmful only when both husband and wife are members of a tainted stock.

Some of the principal varieties of consanguinity in relation to retinitis pigmentosa are illustrated in the following Figures, arranged in groups according to the degree of affinity:—

1. *Marriage of Uncle and Niece.*

Fig. 60. Case from Dr. E. J. Smyth, of Guildford.—Marriage between uncle and niece, both being normal; their respective parents believed to be normal. No. 4 of Generation IV died in infancy, the other six lived to grow up; two affected in six.

* Continuous descent of one or other of these varieties was found in about 120 transmissions within between 70 and 80 families.

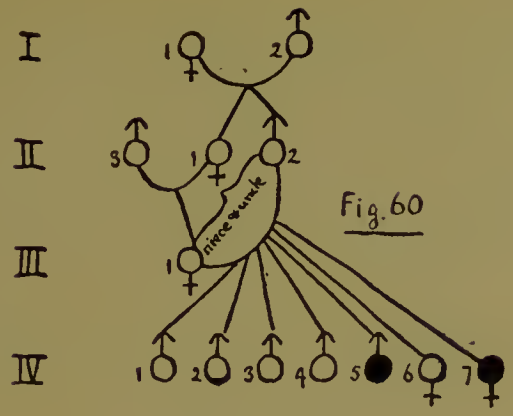


Fig. 72. E. Schmidt's Case 6.—Three affected in a childship of 11, the issue of marriage between uncle and niece (II, 2 and III, 1) themselves and their parents healthy. No earlier information.

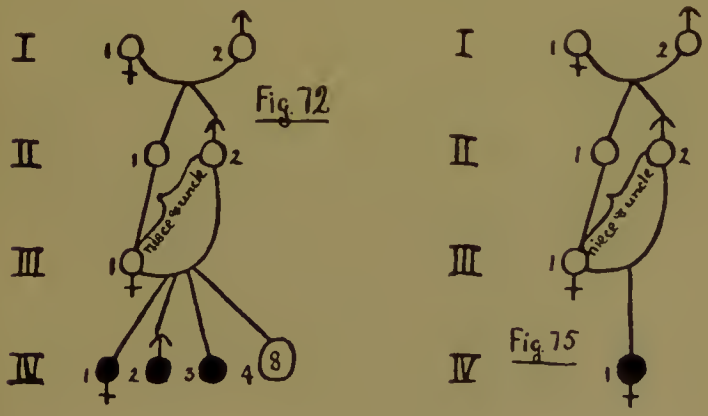
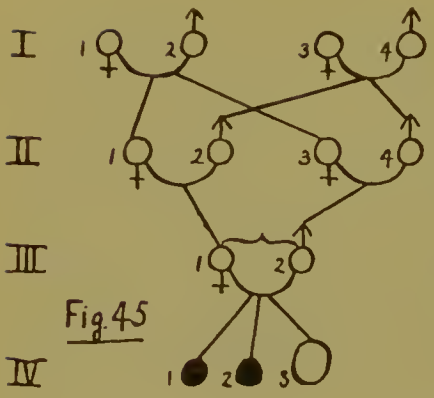


Fig. 75. Mooren (5). Case 17.—Healthy uncle and niece have a daughter with retinitis pigmentosa. No further information.

2. *Double Cousinship of the Parents.*

Fig. 45. Hutchinson (5, p. 6).—The two first-born children of double first cousins affected; no other children born at date of record. No other cases known in three or four generations.



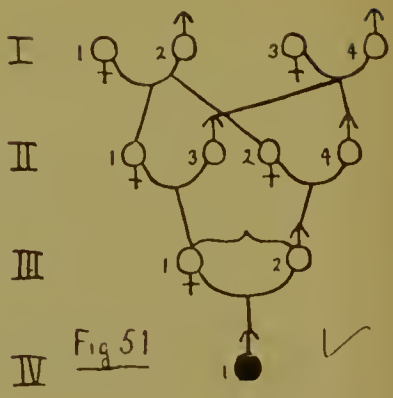
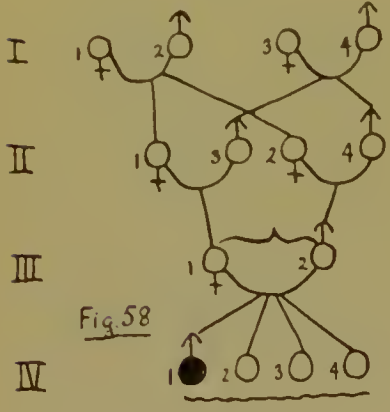
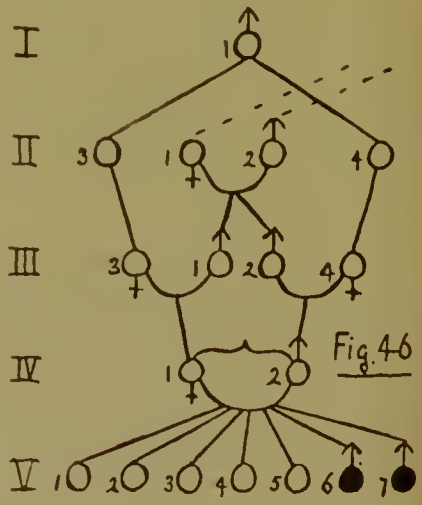


Fig. 51. Another instance of double first cousinship parents. E. Schmidt's Case 27.

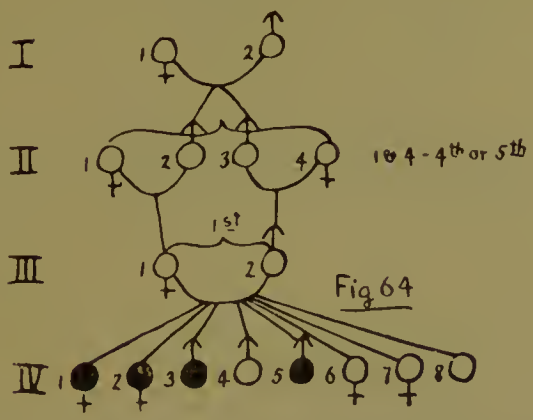
Fig. 58.—Another case in the offspring of double first cousins is Leber's (2) Case 7. One child (IV, 1), æt. 12, affected out of four.





Somewhat similar is Fig. 46, from Herrlinger's Cases 3 and 91; the parents of the patient were first cousins through their fathers (III, 1, 2), and second cousins through their mothers (III, 3, 4), who had a common grandfather, I, 1. No other cases in the family.

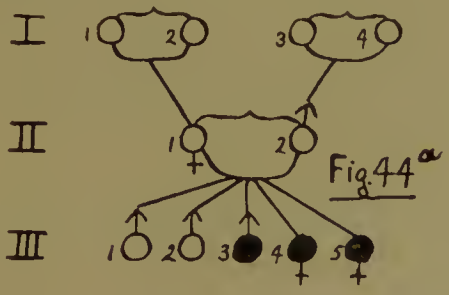
Fig. 64 (P. 31, 67).—At least four children with retinitis pigmentosa out of eight born; youngest (IV, 8) died



æt. 10 months; Nos. 6 and 7 too young for tests. Parents (III, 1 and 2) paternal first cousins and remotely cousins on mother's side also.

3. *Cousinship of Parents and Grandparents* (*Continuous Cousinship*).

Fig. 44*a* (Aubineau).—Retinitis pigmentosa in three out of five children whose parents, being first cousins, were themselves



respectively the issue of cousins; no eye disease known in any ancestors.

Fig. 76 (Treacher Collins's Case).—In a childship of 12, 9 or 10 surviving, four have retinitis pigmentosa (somewhat atypical). Parents, also grandparents on both sides, first cousins; no other cases known.

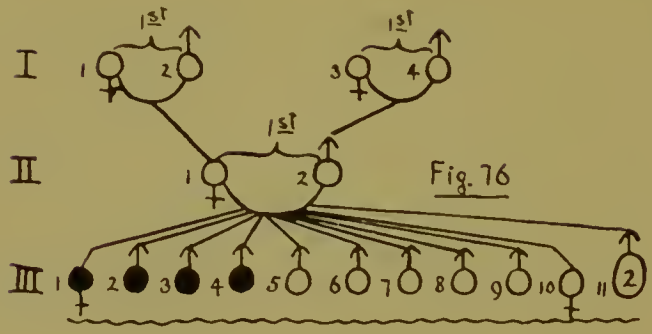
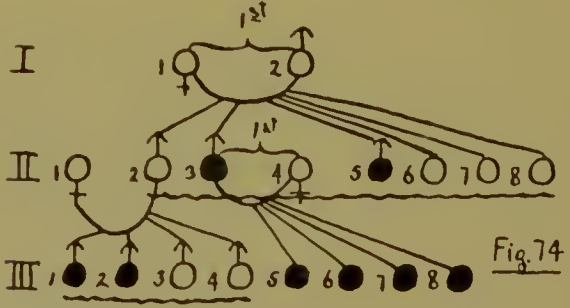
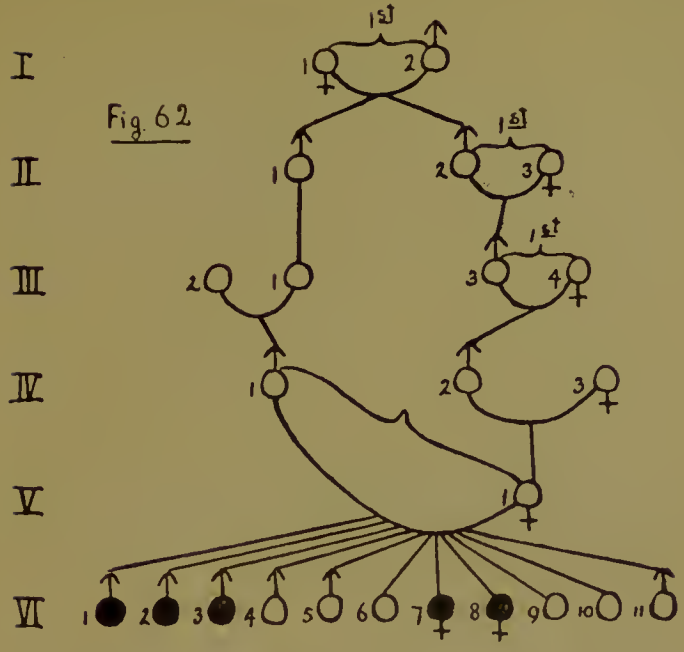


Fig. 74 (Mooren's (5) Case 12).—Consanguinity in (*a*) two successive generations (I, 1 and 2) and II (3 and 4), and (*b*) in one generation with discontinuous descent. In Generation III, two affected childships (cousins). In one of them (1 to 4) two affected out of four and their father (II, 2) healthy and the



son of healthy first cousins (I, 1 and 2). In the other childship all four affected (III, 5 to 8), their father (II, 3) affected and first cousin of his healthy wife (4); father's parents (I, 1 and 2) healthy first cousins.

Fig. 62, one of the most intricate and longest pedigrees of consanguineous marriages, was compiled by Mr. Lawford, who saw the mother (IV, 1) of the affected children, who are patients of Dr. Fletcher, of Highgate. I had also seen some of them several years before. (Mr. Lawford's Case "C.")



Of 11 conceptions in VI, two (9 and 10) miscarried and one (No. 11) died at three years of age and is believed to have seen well. Of the remaining eight, five have retinitis pigmentosa; three of them (2, 3 and 7) are also deaf, and one (No. 3) idiotic in addition. There were at least four cousin marriages in the direct line of the first four generations and no known blindness or deafness or nerve degeneracy. It will be observed, however, that we have no information about IV, 3 the wife of IV, 2, nor about the wife of II, 1, and no particulars of III, 1 and 2.

4. *Parents First Cousins.*

Fig. 44 (Case 7 of Mr. Lawford's series) shows, in an extensive and well-recorded pedigree, a single case of retinitis pigmentosa with deaf-mutism, in one of two children (III, 1, 2) the issue of first cousins (II, 1, 2) whose parents (I, 1, 2) were sisters. These sisters had many other children and many grandchildren, all of whom were known, and known to be free from defects of sight, deaf-mutism, and mental degeneracy It is presumed that there were no other consanguineous

marriages. The history is not known previous to Generation I.

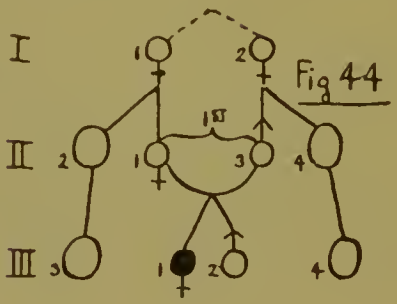
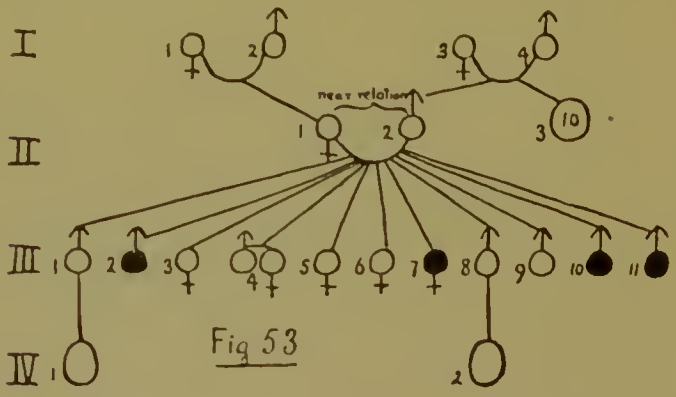


Fig. 53.—Tobin gives a large pedigree in which consanguinity is the only apparent cause, but the record is incomplete as to the mother's sibs and their descendants. All the four



affected ones (of Generation III) were deaf-mute as well as affected by retinitis pigmentosa; they and their eight sibs were all living, including twins; two of them (sons) had children, all healthy (IV).

Fig. 54 (Ancke's Family II, W.) is as follows:—Parents first cousins through their mothers; three children affected out of five, all living.

Fig. 57 (Hutchinson, 4).—Parents paternal first cousins; one child affected out of five, the other four normal. Prolonged illness of father before birth of affected son.

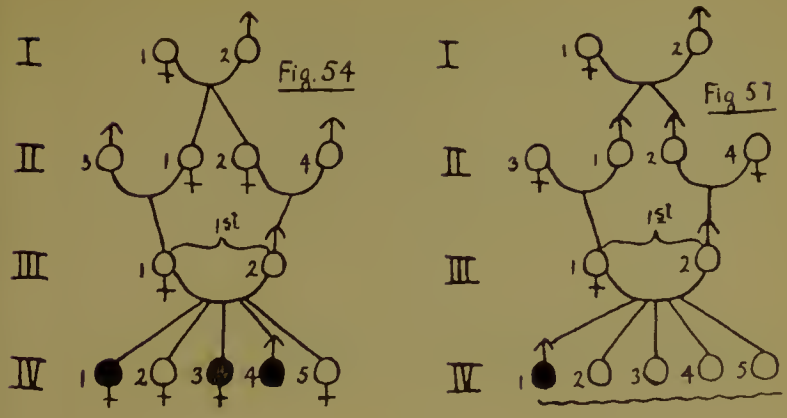


Fig. 55 (W. D. Lee's Family III).—Two brothers marry two sisters, their first cousins. Five out of seven children of the two pairs affected.

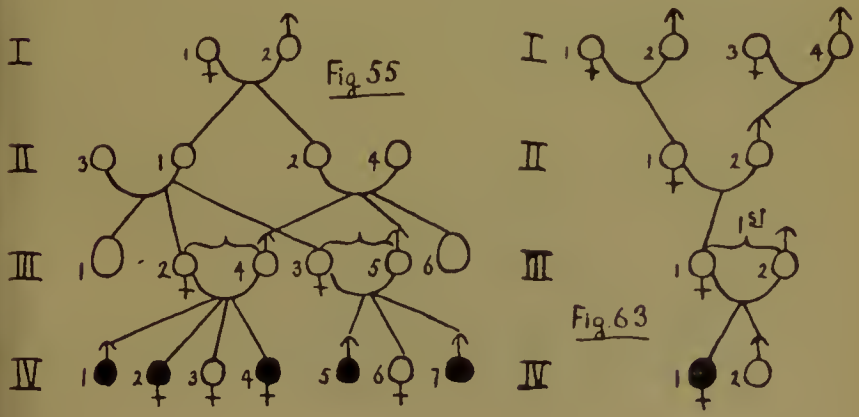


Fig. 63 (my case, P. 21, 54).—First cousins marry and have (1) a girl who has retinitis pigmentosa; (2) a boy, who dies of measles at æt. 2 years, before tests of sight could be applied. History defective on father's side.

Case 71 (Frickenhaus's Family, Becker).—Two out of three children of first cousins affected; the other normal and having three normal children. No other information.

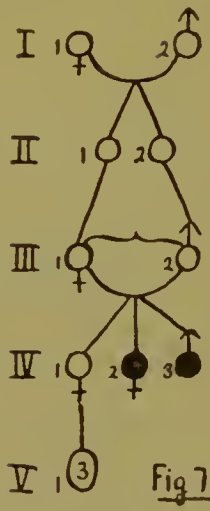
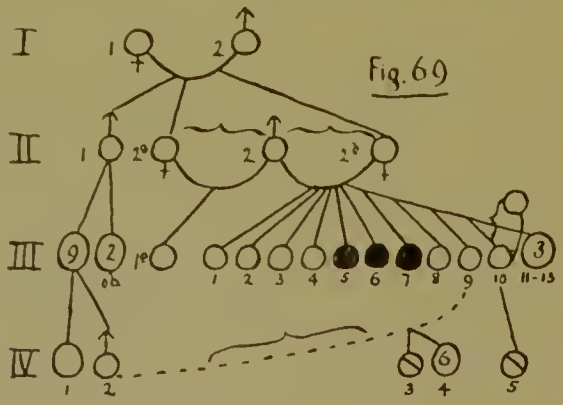


Fig. 69 (Liebreich's Case 1) is of interest not only on its merits, but as being the first pedigree of retinitis pigmentosa drawn up in support of consanguinity as a cause. Generation I, 1 and 2 healthy and not related, had one normal son—(II, 1) whose descendants (in III and IV) were normal—and two normal



daughters (II, 2*a* and 2*b*), who became the first and second wives of their cousin (II, 2). The first wife (II, 2*a*) died at the birth of her first, and still-born, child (III, 1*a*). The second wife (II, 2*b*) had 13 conceptions (III, 1 to 13); Nos. 1, 2, and 3 died in infancy; Nos. 5, 6, and 7 had retinitis pigmentosa,

No. 7 being also idiotic; No. 9 married her first cousin once removed of the same stock (IV, 2), and had seven children, of whom one (IV, 3) was an idiot; No. 10 also married a cousin and had one feeble-minded child (IV, 5); No. 8 married a stranger and had no issue; Nos. 11, 12, and 13 did not marry; No. 4 is not particularised. The family was that of a noble, and consanguineous marriages had been frequent within it for several generations.

5. *Grandparents First Cousins (Discontinuous Cousinship).*

Fig. 49 (Rosenbaum's Cases 8 and 9).—Paternal grandparents first cousins.

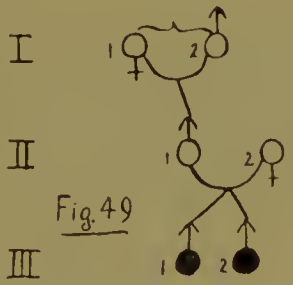
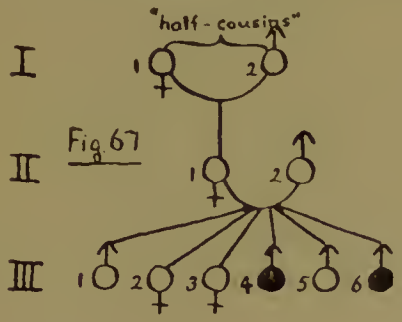


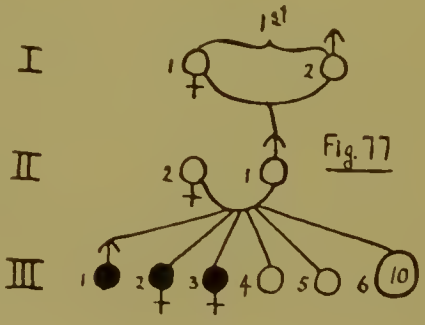
Fig. 67 (my case, M., III, 68).—Arthur Cummings (III, 6), æt. 9, retinitis pigmentosa; No. 4 also affected. Nos. 1, 3,



and 5 examined and found normal. No. 2 died of measles, æt. 1½ years. Mother's parents (I) "half-cousins" and both saw well.

Fig. 77 (Herrlinger's Cases 42 and 43).—Three affected in a childship of 15 (III, 1, 2, 3), of whom only five now living;

no particulars of the 10 who died. Parents healthy and not related. Father's parents first cousins and presumably healthy.



6. *Parents Related, but less than First Cousins.*

Fig. 73 (Herrlinger's Case 71).—Patient, æt. 19 (V, 1), daughter of half first cousins (IV, 1 and 2), the children of half-sisters (III, 1 and 2). No other cases known.

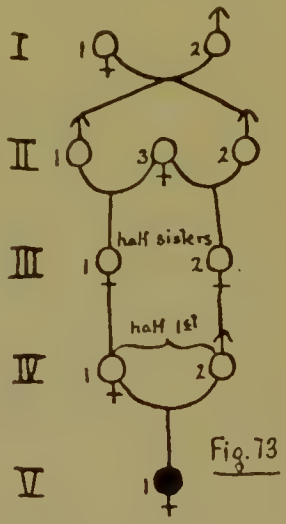


Fig. 48 (Herrlinger's Case 66).—Parents first cousins once removed; the father's father and mother's grandfather being brothers. No other cases.

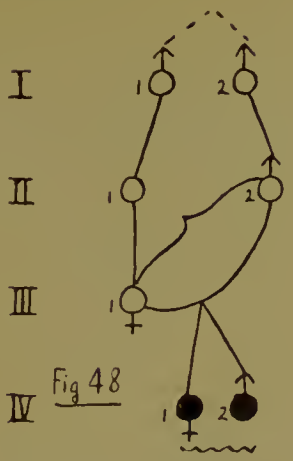
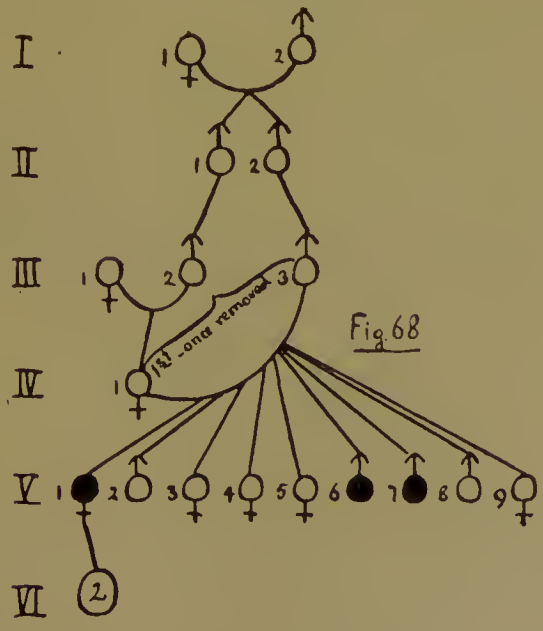


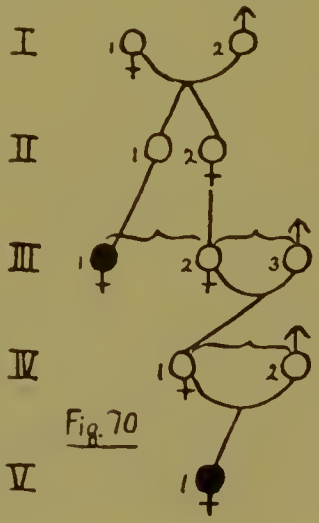
Fig. 68 (my case published, Gould family).—Retinitis pigmentosa, with day-blindness and colour-blindness. Three affected in a childship of nine, of whom eight lived and one (V, 5) died at



11 of "fever." Those affected are Nos. 1, 6, and 7, aged 34, 24, and 21. V, 1 has two healthy children. Parents (IV, 1 and III, 3) paternal first cousins once removed; father (III, 3) died,

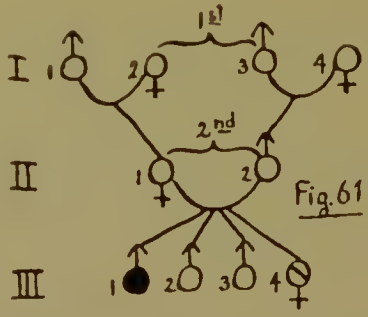
æt. 50, of "heart disease"; mother (IV, 1) married at 22, now about 57, has been melancholic. No information about her mother (III, 1).

Fig. 70 (Huidiez's Case).—Retinitis pigmentosa in daughter, aged 8 (V, 1), of second cousins. No cases in the direct line



for three generations, but a maternal second cousin (III, 1) affected.

Fig. 61 (Mr. Lawford's Case "B.").—Parents second cousins; they and their parents normal. First born of four children



has retinitis pigmentosa (III, 1); fourth born congenital idiot (III, 4).

Fig. 59 (Leber (2) Case 12).—The parents were second cousins,

they and the four grandparents being healthy. Patient (III, 1) æt. 34. No note of other issue.

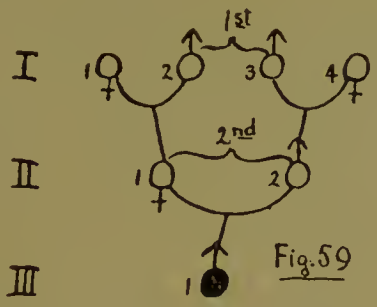
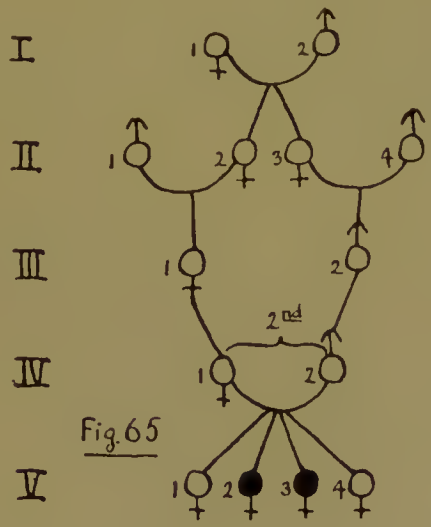


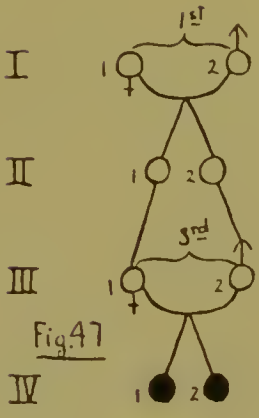
Fig. 65 (my case, P. 37, 215).—Atypical symptoms but typical changes in two out of four children of second cousins; IV, 1, patient's mother was an only child, her mother (III, 1) dying



at her first confinement. No known history of bad sight in Generations I, II, III, or IV, but details of Generation I wanting.

In the next three cases the parents were third cousins:—

Fig. 47 (Herrlinger's Case 39).—The great grandparents of the patients were first cousins; no other cases known.



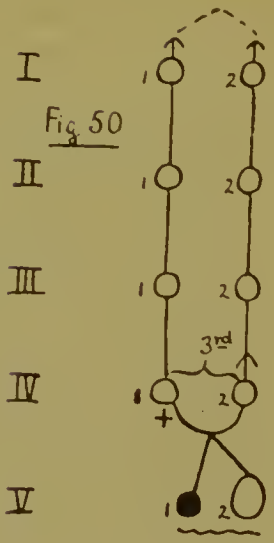
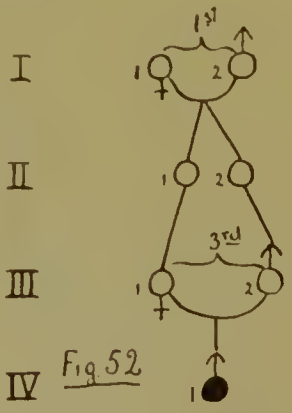


Fig. 50 (Siegheim's Case 34).—Two of the great-great grandfathers of the only known sufferer were brothers.

Fig. 52 (Mooren (5), Case 16).—Two of the great grandparents were first cousins.



A few other numerical questions may be conveniently dealt with here, and the ground will then be clear for looking into certain points in the natural history and clinical characters of the disease, which may throw light on its origin and progress.

Sex in Retinitis Pigmentosa.—All who have collected any considerable numbers agree that many more males than females are found suffering from the disease. Of 1,381 cases in which the sex is mentioned I find 845 males and 536 females, or very nearly 60 males to 40 females. I have made no attempt at present to decide whether these proportions are the same for all ages.

Sex in relation to transmission in the hereditary cases, with or without consanguinity.

(*a*) Continuous heredity, either from parent to child or from uncle or aunt to nephew or niece.

Transmission by the father, in all 36 times, viz.:—

To sons only...	14
„ daughters only	16
„ both sons and daughters ...	3
„ children, sex not stated	3
	36

Transmission by the mother, in all 50 times, viz.:—

To sons only...	18
„ daughters only	15
„ both sons and daughters ...	15
„ children, sex not stated	2
	50

(*b*) Discontinuous heredity — two affected generations separated by one generation entirely free—*i.e.*, transmission by grandparent to grandchild through a healthy intervening generation. I find only eight of these complete enough to be useful; in five of them the disease passed from grandparent, through normal *son*, to grandchild; in three from grandparent, through normal *daughter*, to grandchild. No conclusion can be drawn.

From the above it appears that though there are more living males than females suffering from retinitis pigmentosa, the disease is transmitted oftener by the affected women

than by the affected men, probably because the malady acts as a greater bar to marriage in men than women. We learn, further, that the sex of the transmitting affected parent has no influence on the sex-incidence of the disease in his (or her) children, sons alone being affected about as frequently as daughters alone, whether the affected parent be the father or mother.

(*To be concluded.*)

(*a*) Not-Consanguineous Parentage; (*b*) Consanguineous Parentage.

All childships that were probably incomplete, all in which children died too early for state of sight to be known (except a few in which the proportion of such early deaths to the whole number born was insignificant), and all in which either parent was affected, are omitted.

Number of childships.	Affected.			Not affected.			Total of both sexes.		
	Male.	Female.	Total.	Male.	Female.	Total.	Affected.	Not affected.	
			(*a*) Not Consanguineous.						
93	118 sex not stated	103 21	} 242	115 sex not stated	100 134	} 349	242	349	Average number of children to each childship ..... 6·3 Max. 13. Min. 2. Average number affected in each childship ..... 2·5
							591		
			(*b*). Consanguineous.						
48	61 sex not stated	45 10	} 116	44 sex not stated	46 53	} 143	116	143	Average number of children to each childship ..... 5·5 Max. 13. Min. 1. Average number affected in each childship ..... 2·4
							259		

Thus the average number of children born of each parentage and the average number affected was almost identical for the consanguineous and not-consanguineous marriages.

The proportion affected was exactly or very near to half in each of 32 of the 93 not-consanguineous series, or about 33 per cent. And the proportion affected was exactly or very near to half in each of 18 of the 48 consanguineous series, or about 37 per cent.

The extreme proportions of affected to healthy children in the separate childships were:—

(*a*) Not-Consanguineous Series.

1 affected in 9, 10, or 11 ..... 5 times (minima).
8 „ 11 ..... once } (maxima).
1 „ 1 ..... once }

(*b*) Consanguineous Series.

1 affected in 5 ..... twice (minimum).
1 „ 1 ..... twice (maximum).

i.e., the minimum proportion affected was higher in the consanguineous series; lower and more frequent in the other.

List of Authors Consulted.

All, except those marked *, have been seen in the original.

ABBREVIATIONS.

A. f. A.—Arch. f. Augenheilk. (Knapp and Schweigger).
A. f. O.—Arch f. Ophthalmologie (v. Graefe).
A. O.—Arch. of Ophthalmology (Knapp).
A. d'O.—Archives d'Ophthalmologie (Landolt).
An. d'O.—Annales d'Oculistique.
Am. O. S.—Trans. of American Ophthalmological Society.
Am. J. O.—American Journal of Ophthalmology.
Bul. Q. V.—Bul. de la Clin. Nat. Ophth. de Quinze Vingts.
B. M. J.—British Medical Journal.
C. f. A.—Centralblatt f. praktische Augenheilk. (Hirschberg).
K. M.—Klinische Monatsbl. f. Augenheilk. (Zehender).
L.—The Lancet.
O. H. R.—Royal London (Moorfields) Ophthalmic Hospital Reports.
O. R.—Ophthalmic Review (Priestly Smith).
O. T.—Trans. Ophth. Soc. United Kingdom.
Rec. d'O.—Recueil d'Ophthalmologie.

Dr. Ernest Jones has translated for me several old papers, and all the papers in Dutch, Italian, and Russian, to which reference has been necessary, and my friend, Dr. F. W. Marlow (Syracuse, New York), has sent me some of the less accessible American articles.

Adams. Balt. Med. and Phys. Register, 1809.
Alberrotti. I Ciechi di Collòro. Modena, 1893.
Alt. Arch. f. Augenheilk, vii, 376.
*Alvarado. Revista des Ciencias Med., No. 9, 1882. (C. f. A., October, 1882.)
Ancke. C. f. A., 1885, 167.
Aubineau (with Lenoble). See Lenoble.
Ayres. (1) Am. J. O., 1886, 81; (2) 1892, 65.

Badal. (1) Ann. Mal. l'Oreille, etc., No. 4, 1881 (C. f. A., 1881, 532); and (2) Gaz. des. Hôp., 1876, 1132.
Baumeister. A. f. O., xix, 2, 261 and 272, 1873.
Bayer. Inaug. Diss. Bonn, 1872.
Bellarminoff. A. f. A., 1893, 53.
Van Bierfliet et Van Rooy. A. f. O., x, 1, 81.
Blessig. St. Petersb. Med. Wochenschr., 1902.
Bourgeois et Seguin. A. f. Ohrenheilk, 1876, 182 (On Consanguineous Marriage).
Boudin. Ann. d'hygiene, 2nd Ser., T. xviii, 5, 1862 (On Consanguineous Marriage).

Brochard. Gaz. de Méd. de Paris, 1862.
Bruner. Oph. Record, 1898, August.
*Burstenbinder. A. f. O., 1895, x, 41, 4, 175 (Nagel, for 1895, p. 216, Anatomical).
Byers. Am. J. O., 1900, 11.

Cant. O. R., 1886, 245.
(De) Capdeville. Marseille Méd., 1879, 129.
Chibret. A. O., 1884, 79.
Coleman (W. F.). Amer. Practitioner (Chicago), 1889, 49.
Collins (E. Treacher). O. T., xvii, 53, 1897.
Coröenne. Bul. Q. V., v, 101, 1887.
Cowell. O. T., ii, 58, 1882.

Daguillon. Bul. Q. V., v, 103, 1887.
Darier. A. O., vii, 170, 1887.
Darwin (G. H.). Journ. Statistic Soc., xxxviii, 1875 (Consanguineous Marriage).
Davidson (A. D.). B. M. J., 1886, i, 72.
Denti. Gaz. Med. Ital. Lomb., vi, 113 *et seq.*, 1884.
Derby (Hasket). Am. O. S., 4, 217.
Derigs. Inaug. Diss. Bonn, 1882.
Deutschman. Beitr. f. Aug., iii, 1891 (Sequel of Pedraglia, *q.v.*).
Dolganoff. A. f. A., xxxix, 129.
Donders. An. d'O., xxxiv, 270, 1854; A. f. O., iii, i, 139, 1857.
Dor. (1) A. f. O., xix, 1873; (2) A. O., 1883, 481.

Featherstonhaugh. Am. J. O., 1887, 241.
*Ferret. Bul. Q. V., 1885, p. 32 (quoted by Trousseau, *q.v.*).
Fieuzal. Bul. Q. V., v, 205, 1887.
Frickenhaus. Inaug. Diss., 1873.
Froriep. Neuen Notiz, etc., B. v, No. 3, p. 48, 1838.
Frost (W. Adams). (1) B. M. J., 1889, ii, 1319 and 1419; (2) Atlas, Plate 42 (same case); (3) O. T., vii, 171, 1887.

Goldzieher. C. f. A., 1897, 116.
Gonin. (1) An. d'O., cxxv, 101, 1901; (2) cxxviii, 91 and 128, 1902.
Gould (Geo. M.). Annals of Ophth., 1897, October.
Graefe (A. von). (1) A. f. O., ii, 2, 263, and 283, 1855; (2) iv, 2, 250, 1858.
Groenouw. Graefe-Saemisch Handbuch, 2nd Edition. Lief. 37—38, p. 444.
Gunn (R. Marcus). O. H. R., x, 181, 1882.
Günsburg. A. f. A., xxi, 184, 1890.

Haase. K. M., v, 228, 1867.
Hale. Ophth. Record, 1900, 42.
Hansell (H. F.). Am. J. O., xvi, 153, 1899.
Harlan. Am. Jour. Med. Sci., 64, 130, 1872; and 1873, April.
Heinersdorff. A. f. A., xxxiv, 3, 1898.

Herrlinger. Inaug. Diss. (Tübingen), 1899.
Hersing. A. f. O., xviii, 2, 69, 1872.
Hirschberg. (1) C. f. A., 1889, 37; (2) Berl. Klin. Wochenschr., 1879, No. 47; *(3) A. f. A., viii, 53 (in C. f. A., 1879, 82); (4) Klin. Beobach. etc. Wien, 1874, 72.
Hocquard. Thèse. Paris, 1875.
Höring. K. M., ii, 233, 1864; and iii, 236, 1865.
Hosch. K. M., xiii, 58, 1875.
Huidiez. An. d'O., lxxviii, 211, 1877.
Hutchinson. (1) O. H. R., v, 324, 1866; (2) vi, 39, 222, and 272, 1867; vii, 43 and 434, 1873-4; (3) viii, 54, 1871. (4) Medical Mirror, September 1, 1869; (5) and O. R., i, 2 and 26, 1881 (same case). (6) Arch of Surgery, i, 92, 1890; (7) and ix, 182, 1898 (same case).
Huth. Marriage of Near Kin, 1875.

Jacobsohn. K. M., 1888, p. 202.
Jaeger. (1) Staar u. Staaroperationen, p. 103, Fig. 35, 1854; (2) Traité et Atlas (Wecker and Jaeger), Atlas, Pl. XVII; (3) Traité et Atlas, p. 142, 1870.

Kaupp (Max). Inaug. Diss., Freiburg i. B., 1890.
Kerschbaumer. Die Blinden Herzogtums. Salzburg, 1886.
Knape. A. f. A., 48, 314, 1903.
Knapp. Am. O. S., 1870, 120.

Landolt. A. f. O., xviii, i, 325, 1872 (chiefly anatomical).
Laurence. Old Ophthalmic Review, ii, 32, 1866.
Laycock. Med. Times and Gazette, 1866, April 21.
Leber. (1) A. f. O., xv, 3, 1, 1869; (2) xvii, 1, 314, 1871; (3) Graefe und Saemisch Handbuch, 1st Edition, vol. v, p. 662, 1877.
Lee (Charles J.). B. M. J., 1883, ii, 1184.
Lee (W. D.). The Prænatal Degeneracy of the Eye. Ophth. Record, 1900, 433.
Lenoble (et Aubineau). Rev. Neurol., ix, 393, 1901.
Lewcowitsch. C. f. A., 1897, 253.
Liebreich. (1) Deutsch. Klin., 1861, No. 6; (2) Arch. Gen. de Med., 1861; (3) Atlas of Ophthalmoscopy, 1863.
Lister (W. T.). O. H. R., xv, 254, 1903.
Lopez. Rec. d'O., 1888, p. 553.

*Machek. Przeglad lek., 1881 (Abstr., C. f. A., 1881, p. 382).
McCreight. Annals Ophthalmology and Otology, v, 1, p. 60.
Macnamara. Manual. 2nd Edition.
Maes. Inaug. Diss. Utrecht, 1861.
Magnus. K. M., 1887, 391. Die Blindheit, etc., 1883.
Mannhardt. Klin. Mittheil. aus Constantinople, A. f. O., xiv, 3, 48.
Marlow. Am. J. O., xi, 192, 1894.
Mauthner. Lehrbuch d. Ophthalm., 1868, 382.
Mayerhausen. K. M., xvii, 155, 1879.

Mellinger. (1) K. M., xxvi, 356, 1888; and (2) 1891, 171.
Mooren. (1) An. d'O., xli, 21, 1859; (2) K. M., i, 93, 1863 (repeated in An. d'O., xlix, 254, 1863); (3) Ophth. Beobach., 261, 1867; (4) Ophth. Mittheil. aus d. J., 1874, 83, 1874; (5) Fünf Lustren, 1882.
Mulder. Nederl. Tijdschr., v, Gen. i, 371, 1902.

Netter. An. d'O., lxxv, 198; lxxvi, 198, 1876.
Nettleship. O. H. R., vii, 366 and 552, 1872; ix, 168, 1877; xi, 368, 1887.
Neuffer. Inaug. Diss. (Strassburg) 1893.
Nieden. A. O., xviii, 198, 1889.
Noischewsky or Noiszewsky. Sitz. Mediz. Gesellsch. Dünaburg, 1887.
Nolden. Inaug. Diss. (Bonn), 1876.
Nolte. Inaug. Diss. (Marburg), 1896.

Oakley. Provincial Medical Journal, 1889, p. 329.
Oeller. Atlas, c, Pl. XXV.
Ovelgün. Acta Acad. Nat. Curios. Norimb., vii, 76, 1744.

Pagenstecher (A.). (1) Klin. Beobacht. d. Augenanstalt, Heft 1, 53, H. 2, 26, H. 3, 83, 1861–66; (2) Würtzb. Med. Zeitschrift, iii, 399, 1862.
Pedraglia. K. M., iii, 114, 1865. (See also Deutschmann.)
Peltesohn. C. f. A., 1888, 206.
Perrin. (1) Traité d'Ophthalmoscopie, etc., p. 243, 1872; (2) Perrin and Poncet, Atlas des Mal. profondes de l'Œil, Pls. XLIX and L, 1879.
Picard. Gaz. Med., 1868, No. 23.
Pier d'Houy. Ann. di Ottalmol., vi, 1, p. 10, 1877.
Pisenti. An. d'O., vol. cxxiii, 1900, 354.
Poncet. An. d'O, lxxiv, 234, 1875 (same case as Perrin and Poncet's Atlas, Pls. XLIX, etc., *q.v.*).
Pyle. Am. O. S., 1903, p. 172.

Quaglino. Ann. di Ottalm., xii, 5, p. 372, 1883.

Rampoldi. (1) Ann. di Ottalm., xii, 268; (2) xiii, 507; (3) xiv, 99, 1883-85.
Ransohoff. K. M., 1891, 271.
Reinecke. Inaug. Diss. (Kiel), 1894.
Remak. C. f. A., ix, 257, 1885.
Richter. Inaug. Diss. (Jena), 1828.
Risley. Am. O. S., iv, 226, 1886.
Rosenbaum. Inaug. Diss. (Kiel), 1900.

Sambuc. Thèse (Bordeaux), 1896.
Schelske. Lehr. d. Augenheilk, 167, 1870.

Schiess-Gemuseus. K. M., xiii, 200, 1875
Schleich. (1) K. M., xxiii, 446; (2) xxiv, 469, 1885-86.
Schmidhauser. Inaug. Diss. (Tübingen), 1904.
Schmidt (Ernst). Inaug. Diss. (Bonn), 1889.
Schmidt (H.). K. M., xii, 29, 1874.
Schneider. Inaug. Diss. (Berlin), 1896.
Schoen. (1) C. f. A., 1898. p. 15; (2) Internal. Med. Congr. Paris, 1900. Section Ophthalmology, p. 5.
Schweigger. (1) A. f. O., v, 1, 96. 1859; (2) ix, 1, 205, 1863; (3) Vorles. ü. d. Gebrauch d. Augenspieg., 1864, p. 116; (4) Handbuch d. Spec. Augenheilk.
Seggel. D. Milit. ärztl. Ztschr., xiii, 213, 1884.
Sichel. An. d'O. liii, 1865.
Sieghrim. Inaug. Diss. (Breslau), 1886.
Simi. Old Ophthalmic Review, iii. 278, 1866.
Smith (Priestley). O. R., i, p. 30.
Snell. (1) O. R., v, 73, 1886; (2) O. T., xxiii, 68, 1903.
Spengler. Zeitschr. f. A., vi, 285, 1901.
Steffan. Jahr. ü. S. Augenheilanst, 1873-74, 14.
Stör. K. M., iii, 23, 1865.
Swanzy. Dublin Quart. Jour., 1871, 290.
Szimeni or Scimeni. Ann. di Ottalm., xviii, 69 and 649, 1899.

*Thier. Abstract by Groenouw, in Graefe-Saemisch, 2nd Edition. Lief 37-38, p. 441, 1902.
Tillaux. Un. Med., 1870. 776.
Tobin. Canada Med. and Surg. Jour. (Montreal), xii, 193, 1883.
Treitel. A. f. O., xxxi, i. 139. 1885.
Trousseau. An. d'O., vol. 107, 5, 1892.

Ulrich. (1) K. M., xx, 240, 1882; (2) xxi, 140, 1883.

Van Trigt. Nederl. Lancet, 3 Serie, 2 Jaarg, 492, 1853.
Vieusse. Gaz. hebd de Med., 1878; Z.S., vol. xv, 667.
Voisin. Mem. Soc. Anthropologie, 1866 (Consanguineous Marriage).

Wadsworth. Am. O. S., iv, 227.
Wagenmann. A. f. O., xxxvii, 1, 1903.
Warlomont and Duvez. An. d'O., lxxvi, 113, 1876.
Webster. Am. O. S., 2, 495, 1878.
Wecker. Traité, 2nd Edition, vol. ii, 337, 1868.
Wells (Soelberg). L., 1871, 1, 612.
Wider. Inaug. Diss. (Tübingen), 1885.
Wilson. Dublin Quart. Journ., vol. 40, 72, 1865.
*Windsor. Manchester Med. and Surg. Rep., 1871, p. 161. Translated in An. d'O., lxv, 143, 1871.
*Winselmann. Abstr. in C. f. A., 1902, p. 349.
Wustefeld. Zeitsch. f. A., v, 110, 1901.

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7.

ON RETINITIS PIGMENTOSA AND ALLIED DISEASES.

By E. NETTLESHIP.

(*Continued from p.* 56.)

On Some of the Exciting Causes of Retinitis Pigmentosa.

RETINITIS pigmentosa is the result of a tissue liability present, though seldom manifest, at birth, and known to be so often hereditary that we may be sure it is so also in many cases where the proof is wanting. It is probable that the first changes will be found in the coats of the small choroidal arteries, but this can be neither proved nor disproved until an eye in the early stage of the disease has been fully examined. In the specimen examined by Perrin and Poncet, there were acute inflammatory changes in the choroid, spoken of as metastatic, attributable to the malignant scarlet fever from which the patient (a man aged 21) died, a few days after his eyes had been ophthalmoscopically examined; and these changes masked any choroidal vascular changes that might have existed in relation to the man's retinitis pigmentosa. On microscopical examination pigment granules were found in and amongst the cells of the outer granular layer and the most external part of the outer molecular layer of the retina, but none had reached to the inner retinal layers and consequently none of the retinal vessels were pigmented; Müller's fibres showed some thickening. The man had been night-blind "from birth;" when seen (aged 21) his V. was 12/40 with R., 5/40 with L., Fs. much contracted, colour vision normal, the retina around the disc opalescent and, with the exception of a very few, isolated, stellate dots (microscopical sections of which were not obtained), no pigment whatever was visible under

searching and repeated ophthalmoscopic examination; his father and some other male relations had suffered from night-blindness. The clinical diagnosis of "Retinitis pigmentosa *sine pigmento*" was given.*

We know from the experiments of Wagenmann and others that section of one or more of the posterior ciliary arteries is followed by opacity passing into atrophy and finally pigmentation of the overlying portion of retina; the pigment being derived from the pigmented epithelium and the whole change being due to the atrophy of choroid following permanent interception of its blood supply. Studer† examined the eye of a woman, aged 26, who had undergone optico-ciliary neurectomy a year before enucleation for pain following operation for uveitic cataract, and found the cells of the pigmented epithelium in some parts of the globe not only disturbed but much increased both in number and size, portions of the retina pigmented and the arteries of these portions thickened, and the chorio-capillaris of the corresponding regions either hyperæmic or atrophied. The eye was examined ophthalmoscopically three weeks before the neurectomy and no pigment changes found. If choroidal collateral circulation be quickly established the overlying retina may recover.‡ Studer quotes from Schlodtmann several cases in which the ophthalmoscopic appearances are described at periods from three weeks to seven months after operations for removal of tumours behind the eyeball; pigmentation of the retina was a marked feature in all.

Pigmentation anatomically resembling that of retinitis pigmentosa is often found in eyes that have been blind for a long time from disease of the anterior segment of the globe;

* Poncet, An. d'Oculistique, vol. lxxiv, p. 234 (1875), with illustrations; and Atlas des Mal. profondes de l'Œil (jointly with Perrin), Pl. XLIX (1879).

† Studer (Theodor F.), On Pigmentation of the Retina after Optico-ciliary Neurectomy in Man, Archives of Ophthalmology, vol. xxxv, pp. 333—348 (1906), from the German Edition (with plates), vol. lii (1905).

‡ Knapp diagnosed Embolism of posterior Ciliary Arteries in two cases, and attributed their recovery without residual changes to the free collateral circulation. A. f. O. xiv, I, 207 (1868).

such eyes are generally glaucomatous (Parsons),* and the retinal pigmentation is a consequence of atrophy of the choroid from the prolonged increase of tension. The condition just described is to be distinguished from another series of cases where chronic glaucoma supervenes in an advanced stage of primary (ordinary) retinitis pigmentosa.†

The practical questions are, *first*; whether an hereditary tendency to disease of small arteries, say those of the choroid, may in favourable circumstances remain latent throughout a lifetime? and *secondly* whether any constitutional conditions can act as exciting causes and evoke the changes leading to retinitis pigmentosa in persons some of whom might otherwise have escaped? An hereditary tendency that remained latent would, or might, account for the atavism not infrequently observed in family histories of retinitis pigmentosa (Figs. 17 to 21, p. 19, and other Figs.). In reference to the second question, such a latent tendency brought into action by hæmorrhage or infectious illness may explain the puzzling cases now and then met with where only one member of a large childship suffers. In fact, the belief is often expressed by sufferers from retinitis pigmentosa that an attack of acute illness, especially an exanthem, has either brought out the family liability or accelerated the disease if it had already begun; illustrative examples will be given further on. There is indeed reason for believing that mere loss of blood may in rare instances rival actual division of ciliary arteries in its results and lead to, or greatly intensify, atrophy of the chorio-capillaris and pigmentation of the retina. Such general causes as toxic illness and loss of blood may be supposed capable of operating either by lowering the power of resistance to an already existing dormant tendency, or by inducing independent vascular

* Parsons, Pathology of the Eye, vol. ii, p. 607 (1905).

† Weiss (E.), Retinitis pigmentosa u. Glaukom., in Vossius's Sammlung zwangloser Abhandlungen, &c., der Augenheilkunde, vol. v, pt. 5 (1903). Schmidhäuser, Retinitis pigmentosa u. Glaucom. Inaug. Dissert. Tübingen (1904). (Professor Schleich.)

disease, and probably both processes may sometimes be at work together. It may even be that certain toxic substances produced in the body have a selective affinity for the choroidal arteries, as quinine has for those of the retina.

The effect of copious rapid hæmorrhage in inducing, or stimulating the progress of, retinitis pigmentosa is illustrated by the following cases:—

CASE 77*.—*Severe uterine hæmorrhage at the climacteric period, causing ocular changes that culminated in retinitis pigmentosa. Similar hæmorrhage, causing acute optic neuritis and temporary blindness in a daughter.*

A lady (P. 27.71), whose health and sight had always been good, was confined to bed for several weeks at the commencement of the menopause, at the age of 49, by severe uterine hæmorrhage. The only local disease was a small polypus at the os uteri. This was about May, 1891. During recovery, but whilst still in bed, both eyes failed; all objects, near and far, were indistinct, but she was not blind; it should be mentioned that she was very slightly myopic. A few weeks afterwards, and again six months later (December) she saw Mr. Higgens, who found V. 6/9 in each eye, with the necessary slight correction, no definite ophthalmoscopic changes, but some loss of the upper part of each visual field. In the spring of 1892, a year after the bleeding, and when greatly distressed and shocked by the death of a son, one eye, the L., failed again rather suddenly, and at the end of June its V. was only 6/36. About six months later (October, 1892), when I first saw her, V. of this (L.) eye had improved to 6/12, but objects were distorted, and in addition to a few roundish opacities in the vitreous there was extensive, shallow, transparent detachment of the lower part of the retina reaching just up to the yellow spot, greatest depth, 8 D.; and patches of pigment, accompanied in some places by whitish deposit, were seen in or beneath the detached portion. R. 6/9 with − 1 D., and fundus noted as normal. I did not measure the fields. No complaint of night-blindness.

* Numbering continued from Figure or Case 76 at pp. 37, 38 of the present volume.

Soon after the above date (October, 1892) the L. became slowly worse, and the R. began to fail. I did not see her again until 1897 (aged about 56); the L. had then been quite blind for some time and the R. though still able to see 6/12, had extreme concentric contraction of field (10° to 20° only), and was very blind at night. The ophthalmoscopic appearances were now almost alike in both eyes, and had entirely altered since 1892; extensive pigmentation of retinæ, denudation of pigment epithelium, sclerosis of choroidal arteries—the trunk vessels showing thick white coats—shrinking of retinal arteries, discs pale and waxy-looking, a few opacities in each vitreous, and in R. a small posterior polar opacity of lens; in L. no trace of retinal detachment, but the whitish masses still present between retina and choroid. In 1902, Mr. Higgins found V. of R. still 6/12, and field not smaller, and in 1904 the report was "about the same."

One of this lady's daughters (P. 42.66) suffered from partial loss of sight in both eyes at the age of 23, after copious bleeding from a uterine fibroid; she recovered V. of 6/5 (cm. refraction) in each eye, but when I saw her three months later, there was some loss of F. down-out in the L. eye; and both discs were pale, hazy, and a little swollen, and in the L. the arteries somewhat shrunken.

In the case of the mother just described, the choroidal sclerosis and retinal pigmentation were not found until several years after the uterine hæmorrhage. But the temporary failure of both eyes soon after the bleeding, followed within a year by detachment of retina in one eye, supplies a link, and the phenomena as a whole may fairly be ascribed to disease of choroidal vessels, either initiated or much increased by the loss of blood. That something analogous happened to the daughter is extremely interesting as evidence of the inheritance of very localised peculiarities of structure.

CASE 78.—*Rapid permanent failure of sight with night-blindness after severe hæmatemesis. Advanced retinitis pigmentosa found when first examined several years later.*

George Edmunds (T., O.P., iv, 52), aged 54, a powerfully built man, formerly an engine driver on the South-Western

Railway, came to St. Thomas's Hospital in May, 1882. He was then 54, and said that his sight had been quite good until the events narrated below; but we may take it as certain that the retinitis pigmentosa had been coming on quietly for years before. Married 27 years; no reason to suppose he had had syphilis.

Seven years ago, when about 47, was seized with vomiting of blood whilst mending his engine pumps. The attack weakened him, and when he returned to work he gave up night-duty and drove his engine only by day. Six months afterwards, and again several months later still, the bleeding recurred more or less, and after he had been in bed for a week or two on this account, "something burst again" one morning, and "the blood came up like a pump, two bowls full." During that day his sight failed, and for a few hours he seemed to be in a white fog, and could see no objects; the sight then improved, and kept about the same till we saw him some seven years later, but he never drove his engine again. When seen, May 22, 1882, aged 54, V. of R. was 6/18, L. 6/36; not improved by glasses; pupils acted badly to light; fields much contracted; a small opacity at posterior pole of each lens, and a few round opacities in each vitreous; extreme pigmentation of retina most intense at periphery, but extending in slighter degree almost to the Y.S.; the pigment was in variously shaped spots, round, annular, angular, linear; not a trace of choroidal atrophy, but disturbance of epithelium visible in some places: O.Ds. palish and hazy; retinal arteries moderately shrunken; colour perception slow, but no confusions; hearing good.

In a parallel case by Hutchinson,* a gentleman whose sight had been failing slowly since early life from retinitis pigmentosa underwent, when about 50, and with a year's interval, two severe amputations for diseased bone, the first through the thigh, the second at the hip joint, and on the second occasion he nearly died from secondary hæmorrhage. After each operation he had been "in a mist" for a time, and after the second this was worse, "and he never regained his former sight." Several of his male relatives had had retinitis pigmentosa.

* Hutchinson, Archives of Surgery, vol. ix, p. 182 (Case 32), 1898; and *ibid.*, vol. i, p. 92 (Case 11), 1890.

Mr. Hutchinson adds "it is quite probable that severe losses of blood might be felt by structures already degenerate and with contracted arteries, and not unlikely that such influence might be in some degree permanent."

The patient whose fundus is depicted by Jaeger* in his Hand Atlas was an elderly plethoric man, who assigned the failure of his sight to a period of several years, during which he was losing blood regularly from hæmorrhoids. The appearances, as described in the text, were characteristic of ordinary retinitis pigmentosa, but the illustration is rather atypical, and the history of failure of one eye before the other (if it can be accepted) is unusual.

CASE 79.—*Very severe retinitis pigmentosa, leading to total blindness within about* 10 *years of recognised onset. Uterine hæmorrhage assigned as the cause. Syphilitic arteritis probably contributing.*

Eliza Leeks, an out-patient at St. Thomas's Hospital under Dr. Payne's care, and transferred by him to me (October, 1880), aged 47, married, and had had 15 children, and when 39, about eight years ago, a miscarriage. At the miscarriage she lost a great deal of blood, and both she and the daughter who brought her to the hospital dated the failure of her sight from this flooding; both eyes failed equally. After a time she began to complain of seeing worse in the twilight, and the sight had become much worse during the few months before she came for advice. In October, 1880, aged 47, she could barely see her way about; media clear, the discs yellowish and hazy, retinal arteries contracted to the most extreme degree; retina extremely pigmented from periphery almost to disc, but the Y.S. free; pigment more blotchy than usual, perhaps, only because there was so much of it; no choroiditis anywhere. When seen again three years later she had no p.l. When three years old she had scarlet fever, and had been very deaf ever since; and she had been subject to epileptic fits with tongue-biting since she was about 15. She was one of a childship of nine—five boys, all of whom died before they grew up, three girls (besides herself), all

* Jaeger, Atlas d'Ophthalmoscopie, p. 129, and Pl. XVII, Fig. 79 (1870).

living when the notes were made. She was the only one known to have had bad sight or nervous symptoms. Parents were not consanguineous. She herself had had 15 children, besides at least one miscarriage. One died of consumption, five others died young, and nine were living and reported healthy; one of these, a daughter, was examined, and her eyes found normal. Mrs. L. was in a condition of active tertiary syphilis when we saw her, with nodes on the head and clavicle, and a perforation of the palate. But the eye changes were not like those of syphilis, and we may conjecture that retinitis pigmentosa, beginning early in life, was made rapidly worse by acute, passing into chronic, anæmia of the choroid, due to the combined effects of local syphilitic arteritis and severe systemic hæmorrhage.

Retinitis pigmentosa apparently caused or accelerated by acute exanthemata or other illnesses.—A number of such cases are on record, and no doubt many others have been seen. The most convincing example that I have met with is Case 80 below, but I shall give several others, and refer to some of the best of those that have been published. In many of the hitherto described cases of this class there are central changes either in addition to, or sometimes to the exclusion of, the typical equatorial pigmentation, and in such we find damage to central vision as an early symptom. Cases of retinitis pigmentosa, with relatively severe central loss, have long been known. De Wecker, in 1868, stated that in such cases the retinal disease progressed more quickly than usual, and that they were specially liable to mental complications; I am not aware that this view has been either confirmed or refuted. The alleged influence of acute exanthems on the course of retinitis pigmentosa was briefly mentioned by Leber in the 1st Edition of Graefe-Saemisch (Vol. V), but was not connected with any particular localisation of the changes.

If an acute infectious disease can bring about changes in the choroidal vessels, the same may be true of such chronic fevers as syphilis and tuberculosis. The occasional difficulty of making the differential diagnosis between ordinary or "true" retinitis pigmentosa and chronic progressive diffuse

choroido-retinitis in the subjects of syphilis is well known; and possibly a few of these cases might more correctly be designated retinitis pigmentosa, brought out by syphilitic narrowing of choroidal arterioles. A corresponding position might be claimed for tubercle, but no sufficiently precise data exist as yet for testing the question. There is no doubt, as Dr. R. J. Smyth, of Guildford, pointed out to me in connection with one of his pedigrees of retinitis pigmentosa, that a history of phthisis is common in such families, but the time is not ripe for any attempt to treat the question statistically.

CASE 80.—*In a family of* 10 *children*, 5 *have scarlet fever in early life, followed by retinitis pigmentosa*, 2 *die of the fever*; 3 *escape the fever and have no eye disease.*

In the H. family (P. 6, 89, etc.) we can scarcely doubt that scarlet fever in early childhood was the exciting cause of progressive retinitis pigmentosa in children with unstable nervous system and with consanguinity on the maternal side. In most of the victims the retinal changes differed somewhat from the common form, but in one they were perfectly typical, and, in general, the progressive character of the disease was well shown. The family was under my notice between 1882 and 1904. In the following account the 10 siblings are placed in their order of birth :—

1. ♀ had scarlet fever at 3 years of age; her sight failed in childhood, after the fever, but the exact time of onset uncertain; got slowly worse for a time, but exact state of vision when she died of bronchitis, at 50 (1899), is not known. I saw her in 1882, aged 33, with V. less than 6/60, and with + glasses 6 J. held close; Ps., acted a little; Fs. of full extent; colour vision normal; sight best in bright light; epithelial disturbance all over central area in both eyes, worse in R.; retina at periphery rather hazy but showing no pigmentation; O.Ds. rather pale and hazy; arteries too small. A sleep-walker, eccentric, suffered at times from delusions, and is said to have had Graves' disease at one time. Teeth not suggestive of hereditary syphilis.

2. ♂ born a year after 1. Had scarlet fever when he was 8 years old, *and on the same occasion the five younger children, being*

all that were then born, caught the disease. The sight of No. 2 began to fail just after the illness and got gradually worse. At 22, was able to take his degree at Cambridge, but when I examined him in 1904, aged 54, he could only spell out very large letters with a hand-lens, and for many years had been unable to read ordinary print. He disliked bright light, could go about alone quite easily, and was not night-blind; colour-vision good. Changes in general like those in No. 1, but there were some small collections of pigment on the diseased central area, and sclerosis of some choroidal (short ciliary) arteries. Mental condition good.

3. ♀ two years younger than 2; failure of sight is dated from the scarlet fever. At 23, V. still good enough to be benefitted by glasses for reading; at 26 she married. At 30 (1882) I saw her with Mr. Stanford Morton; V. eccentric, about 16 J.; colour-sense quite good; dislikes bright light; large surface of epithelial loss, with slight pigment collections, at each Y.S. area; border well defined and sinuous; arteries doubtfully shrunken; O.Ds. pale and hazy; refraction H. As. In 1904, reported to be "about the same" and to have three grown-up children with perfect sight.

4. ♀ a year younger than 3; sight became bad, as in the others, very soon after the fever. At 28, could still see well enough to be a governess, and was not blind when she died, at 43 (1897), of heart disease and dropsy; but latterly her mind had failed. I am not sure whether her eyes were ever examined.

5, ♀, and 6, ♀, were aged 4 and 3 respectively when they had the scarlet fever; both died—5 from the fever and 6 from consecutive diphtheria.

7. ♀ was 10 months old at the time of the family epidemic; she was ill at the same time, "either of scarlet fever or measles," and afterwards had "abscess in the ear." Precise date of failure of sight not known; as a child, "could see to read fairly well"; began + glasses at 14. When seen at 24 (1882), well-marked nystagmus, sight worse in bright light, loss of nasal third of each field, with her + sees letters of 6 J. eccentrically. Very typical advanced retinitis pigmentosa extending back to O.D.; O.Ds. more hazy and arteries much smaller than in No. 1, examined at same date. Emotional. In 1904 (aged 36), reported to be nearly blind.

Note that she had the fever at a much earlier age than any of the others, and that her eyes were the worst of any. The nystagmus points to sight having been bad in infancy, probably very soon after the illness.

8, ♂, 9, ♀, and 10, ♂, were born after the scarlet fever outbreak, and never had the disease. In 1904, they were aged from 41 downwards, and all enjoying perfect vision. I had examined the eyes of No. 9 in 1886, when she was 24, and found them healthy; she is extremely hysterical and has more than once been out of her mind.

It may be noted that the mental powers and balance of the three living males (2, 8, and 10) are very good, perhaps rather above the average. The father took to drinking late in life. His wife and he were not consanguineous; she, a healthy woman, was the offspring of "distant" cousins.

CASE 81.—*Atypical retinitis pigmentosa, ascribed to prolonged fever (probably typhoid) Case watched for 12 years. No other cases in the family.*

Frederick Mayhew (M., O.P., i, p. 8), seen at Moorfields in 1882, aged 24, and again in 1892 and 1894. During this period V. sunk in R. (the better eye) from 6/18 and 1 J. with ring scotoma, enclosing clear centre of 10°, to 6/36 and 15 J., with reduction of the clear centre to about 2°. L. was worse than R. in 1882, and did not deteriorate much between then and 1892, when it was about equal to R. The changes described in 1882 had visibly increased by 1894, when the following note was written; the disease is confined to central region and equator, and symmetrical in the two eyes; at equator, chiefly in nasal half, coarse, elongated pigment deposits, many of them conspicuously encrusting the veins; all over the Y.S. area pigment epithelium disturbed, as if the individual cells had joined into small groups, leaving some finer granules between; O.Ds. only slight waxy haze; retinal arteries and veins little, if at all, shrunken. Periphery of fundus free. When 11 years old he had a severe illness, called "slow fever"; his mother says his sight was lost for three weeks during the illness, that it then improved for a time, but soon began to go off again, and has steadily got worse ever since. His own earliest remembrance about it is that he

found he could not see to pick up small things, such as marbles, nor see what he looked at, and that he began to see worse in the twilight. No other cases were known in the family, sight quite good in the mother, aged 60, and her parents, and in the father, who died at 46; nothing known, however, about father's parents, No consanguinity; no family deafness, malformations or defects. Patient shows no signs of hereditary syphilis, and denies having had any venereal disease; he is the third born of 9, 6 ♂, 3 ♀, all living and well, and not one of them, except himself, has ever complained of defective sight.

Case 82.—*Atypical retinitis pigmentosa. Recent rapid deterioration after pneumonia.*

Charles North (O.P. letters), cook, seen at Moorfields, March, 1888, aged 35. Slight failure of sight two or three years ago, but no definite history of night-blindness; could read well until six months ago, when vision failed after a six weeks' illness called "pneumonia and congestion of the lungs," and in two months was as bad as now. Had "typhoid" 15 years ago; denies venereal disease, and shows no signs of inherited syphilis. Has never heard of bad sight in any relations; parents were not consanguineous. Married, wife healthy, and has had seven children, all ♂: 1st, 3rd, and 6th living, aged 10, 5, and 2; the other four died in infancy. On admission, patient's sight, 6/36, Ll.m. 1 D.; with +2 D. reads 14 J. slowly. Fs. of almost full size, but with a ring scotoma about 15° wide, with clear centre of about 10°. Changes exactly symmetrical in the two eyes; (1) a complete zone of pigmented retina enclosing central area, and coming nearly up to O.D., but not extending further anteriorly than the equator, with denudation of corresponding pigment epithelium; (2) an irregularly-shaped area of epithelial disturbance at Y.S. without pigment accumulations; this area more or less definitely separated from the pigmented zone; O.Ds. rather hazy, arteries of fair size, many veins encased by pigment.

E. Schmidt, in his Dissertation (1890), mentions male twins (his Cases 16 and 17) who saw well till they were two years old, when they had measles and diphtheria, and, according to the history, became blind within five months. When examined at

the age of nine both boys were blind of both eyes except in a small sector in the temporal field; changes alike in both, haze of O.D., shrinking of vessels, and fine pigmentation of retina.

Gonin (1901) (Case 3), a girl of 14, with abundant typical retinitis pigmentosa, nystagmus, and very bad sight, in whom the symptoms were dated from typhoid fever at the age of two years. She was the first born of seven, and all the other six (some ♂, some ♀) were said to have perfect sight. No consanguinity, and no cases known amongst relations.

Hersing, in 1872, reported the case of a man, aged 26, whose sight had failed somewhat rapidly after typhus fever in which the cerebral symptoms were severe. Marked night-blindness with some defect of F., but good central V.; at the periphery fine choroido-retinal changes with but little pigmentation; O.Ds. and retinal vessels normal.

Derigs (1882) Case 16, ♂; failure of sight dated from scarlet fever at six years old; saw well till then. Seen at 16 with severe night-blindness and much contracted Fs.; typical retinitis pigmentosa at periphery; elsewhere diffuse atrophy of pigment epithelium and choroidal stroma, but Y.S. exempt. At above date all his seven siblings had perfect sight; but in 1890 one of his brothers, 10 years his junior, was seen at the age of 14 by E. Schmidt, with much contracted Fs. and scanty peripheral pigmentation of retina (E. Schmidt's Case 29). No consanguinity.

In a case by Mellinger (1891) typical retinitis pigmentosa of some, probably long, standing in a woman, seems to have been made worse by an attack of influenza at the age of 51, night-blindness, not previously troublesome, becoming very noticeable soon afterwards. Her four siblings and both parents said to see well. No consanguinity.

Wider (1885) gives three cases in which scarlet fever, and three others in which "typhus" (probably typhoid), was believed by the patient to have brought on the eye disease. The particulars, are very briefly given, and the presence of retinitis pigmentosa in the sisters of one patient, of deafness in the siblings of another, and of congenital absence of arms in a near relation of a third reduces their value for the present purpose.

A similar remark applies to Herrlinger's (1899) Case 7 attributed to measles; both this girl's siblings also had retinitis pigmentosa. For the same reason his Cases 57 and 58 are inadmissible.

The above are only a few of the published cases where the changes leading to retinitis pigmentosa are supposed to have been set in action by an attack of infectious illness. The list might easily be lengthened, but the cases quoted are sufficient to draw attention to the importance of more extended and detailed enquiries in future.

Retinitis Pigmentosa Affecting only one Eye.

In the cases that follow there can be no doubt that the disease was anatomically the same as common binocular retinitis pigmentosa. They can be explained at the present moment only by supposing that the vital endowments of the choroid are sometimes different from birth in the two eyes, an assumption by no means improbable, although unproved. It will be noticed that there is no family history of the disease in any of these uniocular cases. In selecting them I have excluded all in which there is any reason for suspecting syphilis either in the history or the ophthalmoscopic appearances. The only example that I have seen in my own practice is the following:—

Case 83.—Miss A., 30, December, 1894 (P. 32, 243). Perfectly typical and very abundant, retinitis pigmentosa affecting R. eye only; the belt of pigmentation is complete and its anterior limit cannot be reached in ophthalmoscopic examination; O.D. and retinal vessels characteristic; V. with −2 D. 6/18; eye diverges; field not measured. L. V. 6/5, slight H. As.; ophthalmoscopic appearances normal everywhere. She knew that the R. had been "weaker" in sight than the L. even in childhood; no other history. Red hair, fair complexion, teeth very good. Family history was not investigated.

Pedraglia, in 1865, saw a man aged 36, well, strong, and apparently healthy, whose R. eye had been divergent from earliest childhood; the P. was contracted and V. only 6 J. held

elose; media clear; fundus much pigmented from periphery to Y.S. and border of O.D.; O.D. yellowish; retinal vessels only half as large as in other eye, and choroidal vessels sclerosed; in 1891, Deutschmann had the opportunity of examining the eye anatomically. The L. eye had normal sight, full field and fundus perfectly healthy. Parents not consanguineous and no other cases known in any branch of the family. Hereditary syphilis not mentioned.

De Wecker's* case (1870). Girl aged 15, whose L. eye had only bare p.l. and was believed by her parents never to have had sight; it diverged—My. $\frac{1}{4}$ (say 9 D.) in each eye, V. of R. = 2/3 with correction; L. not improved. L. fundus advanced typical retinitis pigmentosa, the Y.S. and its immediate neighbourhood being the only part free from pigmentation; pigment epithelium absent over the whole fundus, but no atrophy of choroid; media clear. R. carefully examined after atropine and no trace of pigmentation found anywhere. Syphilis not mentioned. Nothing as to family history or consanguinity.

Baumeister's case is well-recorded and important from the coincidence of deafness of the ear corresponding to the affected eye. (1873.) It was as follows:—

A man of 44 had well-marked retinitis pigmentosa of the L. eye only, with shrunken retinal arteries and atrophic disc; V. only p.l. and the eye had been "blind" since æt. 12. Since childhood he had also been deaf in the L. ear and Dr. Land reported appearances of past inflammation which might have occurred in childhood or even before birth. The R. eye was normal both as to fundus and V. and not night-blind; and there was no deafness of R. ear. His siblings all normal. There seems to have been some doubt whether the parents were related or not.

Derigs's case (Case 27, 1882), not fully reported, was in a woman of 46 who had advanced retinitis pigmentosa of R. only; eye defective from youth and has steadily got worse; V. now 10/100, F. much contracted, posterior polar cataract. A brother has the same disease but whether in one eye or both is not stated. No consanguinity of parents.

* Traité des Maladies du Fond de l'Œil, par L. de Wecker, accompanied by Atlas d'Ophthalmoscopie, par E. de Jaeger, p. 142, footnote. Paris and Vienna, 1870.

Ancke's case (1885) is somewhat atypical. A boy, aged 15, now in good health but has had diphtheria, scarlet fever, measles with dropsy and "typhus"; no signs of syphilis. Parents not consanguineous. R. eye perfectly healthy as to V., F., and fundus. L. said to have been defective for eight years; now V. about 1/3; F. (taken repeatedly during the next two years) considerably contracted by day and much more so in dull light; typical retinitis pigmentosa towards periphery, but equator thickly sown with bright confluent dots; retinal arteries contracted.

Reinecke (1894) gives brief and not quite convincing particulars of the case of a married woman, aged 44. L. eye defective for a long time but no precise history obtained; now V. = fingers, advanced pigmentation. No changes found in R. eye, but V. with + 1·5 D., only 20/100. No syphilis.

Rosenbaum's Case 34 (1900), given very briefly, was that of a patient, aged 20 (sex not recorded), with retinitis pigmentosa and constricted F. in R. only. L. fundus normal. No other particulars.

Case 9 in Gonin's second paper (1902) is one of typical advanced retinitis pigmentosa with very bad V., confined to the L. eye, in a man aged 25; the eye was said to have been bad from childhood and had been examined and pronounced incurable at Strasburg some years before Gonin saw the patient. R. eye normal in every respect except H.As. No consanguinity of parents; no other cases known in relations. Had scarlet fever (? measles) some years ago, but the eye appears to have been bad before that. Four of patient's siblings died young and their father died suddenly at 34; these are the only recorded facts pointing to syphilis. A younger brother of patient had perfect eyes.

I reject Mooren's often quoted case in a woman of 35 (1867) since he expressly states that although visible pigmentation was confined to the L., the R. showed "rather scantily developed" retina and optic nerve and a much constricted F.

Neuffer's case (1893) is also omitted because (1) there was disease of vitreous and perhaps detached retina; (2) a sister had choroiditis; and (3) syphilis is not mentioned.

(*To be concluded.*)

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ON RETINITIS PIGMENTOSA AND ALLIED DISEASES.

By E. NETTLESHIP.

(*Continued from p.* 166.)

(References to previous cases and pages mean cases and pages in the earlier portions of this paper.)

THERE is no lack of *fertility* in healthy parents who have children afflicted with retinitis pigmentosa, nor in those subjects of the disease who themselves become parents. Amongst about 195 apparently completed childships containing cases of retinitis pigmentosa, I find 96 in which from 7 to 19 children were born; the total number born was 878, giving an average of 9 to each marriage; the most frequent number or "mode" was 9, the same as the average, 22 childships having this number. Whether the prolificacity here indicated is greater than the normal in the different populations and various social grades from which the material was drawn, I have no means of knowing; but as the records were made some years ago, when intentional restriction of births was probably much less common than it is believed to be to-day, fresh statistics made some years hence might not show so many large childships. A high birth-rate has been noticed in some other family peculiarities, eye-diseases* and affections of the nervous system,† and recently Karl Pearson‡ has shown that in phthisis the fertility is certainly not lower, probably higher, than normal.

Again, the subjects themselves of retinitis pigmentosa, if

* Hutchinson, Archives of Surgery, I, p. 300, footnote (1890).

† James Taylor, O.T., vol. xvii, p. 63 (1897).

‡ Karl Pearson, A First Study of the Statistics of Pulmonary Tuberculosis, p. 20 (Drapers' Company Research Memoirs) (1907).

they marry, not infrequently have many children, in spite of the economic difficulties caused by the increasing failure of sight, difficulties that might be expected to act as a check upon the later births, especially if the affected parent be the father. Cases in point are mentioned by Monoyer;* in Snell's recent case† an affected mother had 9 children; and in his earlier case† (Fig. 2 of the present paper, p. 10), two affected fathers (themselves father and son) had 11 children each; in one of Schneider's cases (Fig. 3 of present paper), an affected mother had 11; Fig. 1 (p. 8) shows one affected mother with 12 children, one with 9, one with 8, and two with 7 each, whilst no affected father had more than 5; in Fig. 11 (from Ransohoff) and Fig. 12 we see affected mothers bearing 7 and 8 children respectively, and in Fig. 104 below‡ two affected mothers had 12 and 9 respectively and two affected fathers 9 each.

It may be observed further that in several instances of great prolificacity the parents of affected children have themselves been children of prolific marriages.

Early Deaths, Premature Births, and Miscarriages are of course recorded in a certain number of the families, but the data are much too scanty to justify any conclusion, and I give them merely as an inducement to the collection of more material in future. In each of 24 affected childships consisting of 6 or more conceptions, there were 2 or more early deaths; whilst in only about 10 childships of less than 6 each was there an early mortality of 2 or more. Such figures afford no support to the contention, should it be made, that retinitis pigmentosa is correlated with high infant mortality: they only show that the number of early deaths is larger in large than in small childships.

"*Anticipation*,"—the appearance of the disease at an earlier age in each succeeding generation—seems scarcely

* Monoyer, Ann. d'Oculistique, vol. lviii, p. 143, in a note to his Abstract of a paper by Höring.

† Snell, Trans. Ophth. Soc., vol. xxvii, p. 217 (1907); *ibid.*, vol. xxiii, p. 68 (1903).

‡ Already published in part as Fig. 6, p. 13.

ever to occur in retinitis pigmentosa; or if it do happen it cannot be proved, because the onset of the malady is so gradual that its date can seldom be fixed with any approach to accuracy. The history usually points to the night-blindness having been noticed at about the same age in each generation: very early in life in some pedigrees, rather later in others. But cases showing anything like decided anticipation are so rare that they must, with our present knowledge, be taken to be accidental. In fact, the only good example I have found is Darier's Case 2 (1887), in which the symptoms are said to have been first noticed in the father at about the age of 34, and in his two affected children at 8 and 15 respectively.

The absence of decided "anticipation" is well illustrated by such cases as the following:—Daguillon; a man (grandfather) was night-blind from the age of 19, his daughter from 10 with advanced disease at 39, whilst two of her three children showed the disease at 11 and 7 respectively. Hutchinson;* a father dated his symptoms from the age of 18, and his daughter had characteristic changes at 19. Ayres' cases, Family III; the mother, æt. 37, had had symptoms since childhood, and her two daughters showed typical changes at 15 and 12. My case (Fig. 6A, p. 14); history that the disease set in very early in life in Gen. III as well as in Gen. IV. In Cases 1 and 2 (p. 8 *et seq.*), both long pedigrees, the symptoms began early in life in all the generations so far as could be ascertained. Many similar cases could be quoted.

It would be interesting to know whether the *kind of cousinship of consanguineous ancestors* has any bearing upon the occurrence of the disease in their descendants, but very little material is available. As a rule, we think we have done our duty by noting "parents first cousins," and seldom go on to ask whether the consanguineous parents were children of two brothers, of two sisters, of brother and sister or of sister and brother. The following are the only cases I have been able

* Hutchinson, these Reports, vol. vi, p. 39.

to collect. It will be very easy for observers to accumulate such material in the future in connection not only with retinitis pigmentosa, but all conditions in which consanguinity is frequent. Victims of retinitis pigmentosa whose father and mother were children of brothers, three cases (Herrlinger's Case 3, Hutchinson's case, Fig. 57, p. 41, my case, Fig. 64, p. 37); father and mother the children of sisters, four cases (Ancke's Family W., Fig. 54, p. 40, his Family B., Lawford, Fig. 44, p. 39, my case, Family Dow, unpublished); mother's father and father's mother were siblings (Hirschberg, 4). Mother's mother and father's father half siblings by same father and different mothers, one case (Neuffer's, 13A); mother's mother and father's mother half siblings by same mother and different fathers *who were brothers*, one case (Herrlinger's Case 71). Mother's father and father's mother half siblings by same father and different mothers who were not related to each other or to their husband, one case, Lawford (Fig. 61, p. 46).* The two grandfathers of the patient were brothers and the two grandmothers sisters, *i.e.*, patient's parents double first cousins, three cases (Schmidt, Fig. 51, p. 36, Hutchinson, Fig. 45, p. 35, Leber, Fig. 58, p. 36). The two grandfathers of the patient were brothers, the two grandmothers first cousins (Herrlinger, Fig. 46, p. 36). The two grandfathers first cousins (Leber, Fig. 59, p. 47). The father's father's mother and mother's father's† mother were sisters, Fig. 65, p. 47. Patient's father's father and mother's grandfather were brothers (Herrlinger, Case 66); patient's father's grandmother and mother's grandfather were brother and sister, patient's mother's grandmother and father's grandfather were brother and sister (Herrlinger, Case 33). Patient's father and mother, uncle and niece (Herrlinger, Case 75, Mooren, Fig. 75, p. 35, Trousseau, Schmidt, Fig. 72, p. 35, Neuffer, Case 1, Dr. E. J. Smyth, Fig. 60, p. 35, La Gleyze, Fig. 35, p. 28): aunt and nephew one case (Peltesohn).

* The pedigree, as shown by Fig. 61, is wrong; it has been corrected by the patient to the form above described since Fig. 61 was published.

† III, 1 in Fig. 65 should be ♂.

There is a similar scarcity of information as to the *age of the parents at marriage*; in Fig. 1 the affected woman, V, 20, was about 21 when her first child (VI, 22) was born, 25 when VI, 24 who is affected, and about 37, when VI, 26, also affected, was born. In Badal's case a woman marries at about 25, when in an early stage of the disease, has a seventh month child that did not live, then two children who were normal at date of writing when mother was 41 and her V. much worsened; children would then be about 12. In a case of my own (P. 55, 18), a man of 60 marries a woman of "about 50," not related; the only child, male, has retinitis pigmentosa; no known case of the disease in earlier generations, but family history incomplete. In my case of Miriam Tyley (St. Thomas's Hospital) the father was about 21 when he married; he had only two children: first, a boy, healthy; second, girl, Miriam, born when her father was about 27, and seen at the age of 17 with retinitis pigmentosa. In Dr. Maude's case (Case 83H) below, the mother married at 18, and the father at 21. In my case of Bramston (St. Thomas's Hospital), an illegitimate child, the mother was 15, but there is no record of the father. In Mr. Lawford's Case 6, the father was 25, the mother 27. And it is of course true as a general statement that the very large childships imply early marriage.

Attention has already been asked (p. 153) to a possible explanation of those *cases in which we are told that only a single member of a large sibship* (*childship*) *has developed the disease*. Such cases are not common, and, in addition to those quoted at p. 153, and Case 83I below, I find only the following, in which all the siblings of the patient were not only free from retinitis pigmentosa and its equivalent degeneracies, but old enough to render the subsequent occurrence of such very improbable, and in which it is believed that the number of offspring recorded represents all the conceptions.

CASE 83A.—Martha Craxton, aged 24, 1895 (Moorfields Hospital); black hair; characteristic retinitis pigmentosa with

deep haze of the pigmented belt and disturbance of pigment epithelium on the corresponding parts, shrinking of retinal arteries and brownish haze of disc; periphery free; Fs. show well-marked annular scotoma; V. with slight As. corrected 6/6 in each; Bjerrum's types 6/18; has been dusk-blind as long as she can remember, and does not think she is getting worse. Is 3rd born of 8, all living, and all see quite well; No. 4, also a girl; the other 6 are males. No consanguinity and no other cases known. CASE 83B.—Emily Thorne, 13 (Moorfields, I.P., 1899); is 3rd born of 4, ages of the others 18, 16, and 12; sexes not recorded. Typical changes; symptoms since she was about 5. No note as to illnesses; no signs of inherited syphilis. No consanguinity and no other cases known. Fig. 43 (p. 31) shows a man aged 43 (III, 2) with retinitis pigmentosa, the only case in a childship of 9; sexes and order of birth not recorded; nothing said about illnesses. CASE 83C.—(Schmidt's Case 1); man aged 40; symptoms began after "typhus" at 15; was one of 11, of whom 3 are living, the other 7 having died at advanced ages; order of birth and sexes not recorded; none had the disease except himself; no consanguinity or known family history of the disease. CASE 83D.—(*Ibid.*, Case 33); woman aged 32, one of 5; 3 ♂, 2 ♀, all living, and all with perfect sight except herself; no further information. CASE 83E.—(Frost, 1 and 2); woman aged 23; 3rd born of 5; no consanguinity of parents. CASE 83F.—(Harlan, Case 6); woman 22, one of 13, 3 ♂, 10 ♀; the other 12 all see well; order of birth not given. Parents consanguineous, but exact degree not stated.

On the other hand, such a case as Fig. 40 (p. 30 above) shows how deeply latent the disease may be, and should induce extreme caution in attributing anything more than an exciting influence to such agencies as those illustrated at p. 154, etc.; unless IV, 4, in Fig. 40, aged 26, had known of the deaf-muteness in her great-aunt (II, 1), no trace of heredity could have been shown in the pedigree.

Relation between Sex and Age in Retinitis pigmentosa.

At p. 49 it is stated that, in a total of 1381 cases in which sex is given, there were 845 males and 536 females,

or very nearly 60 males to 40 females, precisely 61·2 males to 38·8 females. In the above total of 1381, the number of those whose age is stated either exactly or approximately is 1025, consisting of 640 males and 385 females, or practically 62 to 38, proportions practically the same as those of the larger aggregate.

We may therefore use the total 1025 with safety as material for enquiring whether the proportion of males to females differs widely at different ages, and, although the numbers may not be final, they are large enough to have some value. For the purpose in view, the 1025 cases have been classified from 5 years of age upwards, as far as possible into quinquennial periods, from 1 to 5 years old upwards to 85 to 90; a certain number which could not be placed in any one such period could be classed only as more or less than 20 years. The result is as follows:—

(1) There are 18 quinquennial groups, containing 889 cases, males 565, females 324, or very nearly 64 males to 36 females. (2) In the 18 quinquennial groups the males exceed the females in all but two, and these two groups are so small as to be negligible, viz., aged 71—75, ♂3, ♀4; aged 81—85, ♂1, ♀1. (3) In the cases classed merely as over 20 years old, there are 108, 60 males to 48 females, or 56 males to 44 females. (4) Those classed merely as under 20 number 28, males 15, females 13. (5) Adding those in the four quinquennial periods below 20 to the above 28, we get:—

Sex in Subjects of Retinitis pigmentosa below 20 Years of Age.

	♂	♀	Total.
Total of 4 quinquennial periods below 20	175	130	305
Others classed only as under 20.....	15	13	28
	190	143	333
	58	42	100

(6) Adding to those in the 14 periods beyond 20 the 108 above, the corresponding figures are :—

	♂	♀	Total.
Total of 14 quinquennial periods, aged over 20	390	194	584
Others classed only as over 20.....	60	48	108
	450	242	692
	65	35	100

Comparing the periods above treated we have :—

	All ages.		Below 20.		Above 20.	
	No.	Per cent.	No.	Per cent.	No.	Per cent.
Males	(640)	62·5	(190)	58	(450)	65
Females	(385)	37·5	(143)	42	(242)	35
	(1025)	100·0	(333)	100	(692)	100

Thus the excess of males over females is rather less in those under than in those over 20 years of age.

The actual proportion of males to females living in the populations of three European countries, as given in Whitaker's Almanac, 1908, is as follows, in millions* :—1. England and Wales, Scotland, Ireland, and the home islands (1901), ♂ 20,171,000, ♀ 21,434,000. 2. Belgium (1904), ♂ 3,514,000, ♀ 3,560,000. 3. German Empire (1905), ♂ 29,884,000, ♀ 30,756,000. Or reduced to uniformity :—1. In England, etc., for every 1000 living ♂s there are about 1062·5 living ♀s. 2. In Belgium, for every 1000 ♂s there are about 1013 ♀s. 3. In German Empire, for every 1000 ♂s there are about 1030 ♀s. The greater number of the cases collected for the present paper are from England and Germany; if, therefore, we put the proportion of the sexes living in the

* Whitaker does not give the numbers of the sexes separately for any other countries.

populations from which the material is derived as about 1000 males to 1050 females, we shall probably not be far wrong.

If the proportion of males to females in retinitis pigmentosa were the same as for the above estimated normal average, the 1381 cases of the disease should have contained 674 males (instead of 845) and 707 females (instead of 536). There must therefore be a considerably greater incidence on the male sex, unless there be some source of error, such as concealment of the disease by females, which is extremely unlikely; or, what is less improbable, a disproportionate number of infantile deaths amongst the females of affected childships, *i.e.*, death of a number of females who would have shown the disease had they lived; or it might be simply that the disease occurs most in those childships that contain an excess of male births.

Although my data are not complete enough to decide such points, the following results may be recorded for what they are worth: in 54 completed childships, where the sexes were fully noted, the males born were to the females born as 239 to 119, or 67 males to 33 females (100); the cases of retinitis pigmentosa were 140, males 102, females 38, or 73 males to 27 females (100), an excess greater than the excess of males born. In 29 other childships, more females than males were born, as 137 to 58, or 70 females to 30 males (100); 72 had retinitis pigmentosa, 41 females, 31 males, or 56 to 44 (100), an excess much smaller than the excess of females born. In 16 other childships the number of males and females born was equal, 30 of each; 32 of the total 60 had the disease, and, curiously, only 10 of these were males, 22 being females; but this series is too small to be of much value.

The possible relation between sex and retinitis pigmentosa may also be tested by comparing the completed childships in which all the diseased siblings were male with those in which all were female; single births and childships consisting entirely of affected children excluded. This shows, to begin with, 31 childships with only males affected against

11 with only females affected. The 31 contain 148 individuals: 59 affected males, 44 males and 45 females healthy. The 11 contain 25 individuals: 14 affected females, 5 females and 6 males healthy. These figures show, as far as they go, that when only one sex in a childship is attacked, it will be the sex that is most numerous. They also illustrate afresh the already known greater incidence of the disease in the male. This greater incidence in the male also appears if we count the childships in which every child had the disease; there are, in my material, 14 all male childships with every child affected, total 24; but only 4 all female childships with every child affected, and the total only 5.

Can anything be learned about the cause either of retinitis pigmentosa or its equivalents by examining *the relative order of birth of the healthy and diseased children?*

Berry* pointed out, in his remarkable case of hereditary cataract, that the disease usually attacked several successive children, as if the mother had been more liable to transmit it during one particular period of her child-bearing life than at others (as transmission in Berry's case nearly always occurred through the affected mother, we cannot suppose that the age or health of the father would exert any influence). In the material at my disposal I find 45 childships (no more) in which, the true order of all births being given, two or more children *born in succession* were affected, either all of them by retinitis pigmentosa, or some by it and others by one or other of the equivalent degeneracies. These 45 childships show that the subjects of simple retinitis pigmentosa, and of that disease with added deaf-muteness, are not infrequently born in succession to the numbers of two and three, and in one instance four; and that if "equivalent" or "substitute" degenerations, premature births and very early deaths, be classed with retinitis pigmentosa, the groups of successively born degenerates so formed are often much larger. But the same data show also that solitary

* Berry, Ophthalmic Review, vol. vii, p. 1 (1888).

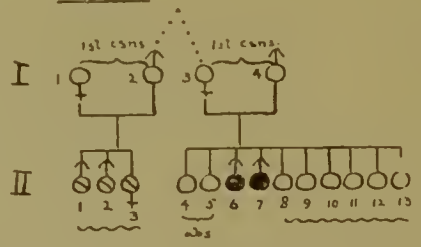
instances of retinitis pigmentosa, separated by one, two, or more normal siblings, are fairly common, and that such solitary cases may appear either in the van or rear of a group of affected siblings. There is perhaps a tendency for the degeneracies, when successive, to attack the earlier rather than the later births; *e.g.*, this occurred in Fig. 69 (p. 42), if the order of birth of the 13 children is correct; in addition to the history there given, III 4 died paralysed, æt. 16. But the number of families available is too small for a numerical statement, and in several cases, where a majority of the children have been affected in one way or another, the different degeneracies have occurred in irregular order. For example, in a case by Sambuc there were 14 conceptions, 8 ♂, 4 ♀, and 2 sex not stated; 6 of the 8 males (Nos. 1, 2, 8, 9, 10, and 12) died under 3 years of age; 2 males (Nos. 3 and 7), and all 4 females (Nos. 4, 5, 6, and 11), survived, and had retinitis pigmentosa; Nos. 13 and 14, twins, sex not stated, died at a few months old. In the case of a family named Pearce (these Reports, vol. ix, p. 173), 15 children out of 18 died very early, and the 3 survivors, who were amongst the eldest born, all had retinitis pigmentosa. Fig. 28 (p. 23) shows a childship of 19; 10 died in infancy, No. 5 was an idiot and died young, Nos. 6, 12, and 13 had retinitis pigmentosa and were alive at from 30 to 40, whilst Nos. 1, 8, 11, 14, and 15 all grew up and were said to have been healthy, though three of them died as young adults from various accidental diseases.

The list of the *degeneracies* of the central nervous system, congenital defects, and arrests or malformations that occur in the subjects of retinitis pigmentosa or their siblings, or other near relations, is well known to be a long one. The commonest is congenital (or at least very early) deafness of various degrees; when complete, associated with dumbness. Congenital idiocy and the varieties of mental deficiency, insanity, and epilepsy come next in frequency. Then a few cases of progressive paralysis, apparently spinal, perhaps not yet thoroughly analysed. Polydactylism,

coloboma iridis, remains of the hyaloid artery, congenital cataract, and conical cornea, are recorded by several authors; whilst in single cases, a peculiar condition of the skin, heterochromia iridis, colour-blindness and posterior cortical cataract without other changes, have been seen. Congenital cataract (variety not stated) was seen by Professor La Gleyze in some cousins of one of the unpublished cases that he has kindly sent me :—

Case and Fig. 836 (La Gleyze, unpublished cases, No. 51).—II, 6 and 7, two brothers with retinitis pigmentosa, aged 12 and 10 (1903); two earlier conceptions (4 and 5) ended in abortion; 8 to 13, six other children, no details. II, 1, 2, 3, three siblings, first cousins of II, 6 and 7, affected by congenital cataract; one was operated, and the fundus, when examined afterwards, was normal. Not only were the two childships in II cousins, but their respective parents, I, 1 and 2 and I, 3 and 4 (all quite healthy), were so too.

Fig. 836



Twins were recorded twice in my own series of cases (about 120 families). Occasionally more than one morbid condition is found besides the retinitis pigmentosa; for example, in Herrlinger's Case 22 three siblings with retinitis pigmentosa were all idiotic, and two of them had also supernumerary digits; a brother of their father was deaf-mute as well as blind, and a more remote paternal male ancestor had also been deaf-mute. Tobin records retinitis pigmentosa with deaf-muteness and a twin birth in the same childship. Arterial disease may have taken a share in Cases 831 and 104 given at p. 347. Exophthalmic goitre

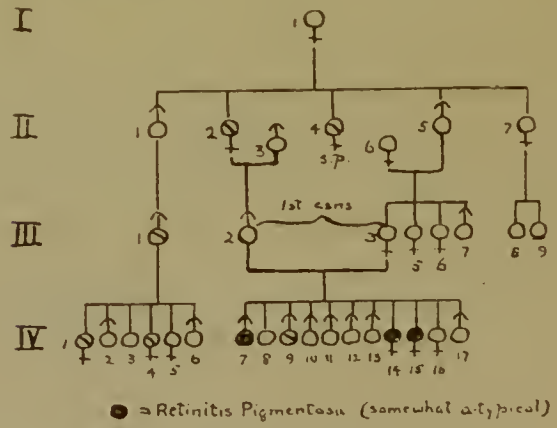
occurred either in the subject of retinitis pigmentosa, or in some relation, in three families; one by Mooren (5) in a deaf-mute with retinitis pigmentosa aged 30, my Case 80 (p. 159), and Case 83H, kindly sent to me by Dr. Arthur Maude.

CASE and Fig. 83H.—*Retinitis pigmentosa, with Graves's disease and various degenerative neuroses in other members of the genealogy.* Dr. Arthur Maude's case. I, 1 died of epithelioma of vulva, at advanced age, in 1888; mental condition good; had five children, apparently all normal sighted; all married, and four of them had issue; only one (II, 4) had no children; she was extremely hysterical. II, 1 had a son, III, 1 who is half-witted, and now aged about 47 (1908); he has six children, IV, 1 to 6, of whom IV, 1 is a congenital imbecile, and IV, 4 had infantile fits. II, 2 and her husband, II, 3, both alcoholic and very arthritic; II, 2 had Graves's disease, complicated at one period by partial double ptosis and paralysis of fourth, sixth, and facial nerves on left side (probably nuclear);* became very arthritic; still alive. She had at least one son (III, 2), also more or less alcoholic. II, 5 and his wife (II, 6) had good sight; they had four children (III, 3 to 7); III, 5 and 6 are unmarried, and aged about 37 and 34 (1908); III, 7, no information. III, 3 married her first cousin, III, 2, when she was 18 and he 21; both became too fond of alcohol; no history of syphilis in either of them, but the husband (III. 2) when 27 (1892) had a febrile illness with a fleeting eruption, mainly roseolous, partly herpetic, effusion into knees and ankles for a short time, and purulent urethritis, the latter subsiding into chronic gleet; the wife (III, 3), when seen in 1906, aged 38, had normal vision and perfectly healthy fundi; she died in 1907 of uterine carcinoma; she had 11 conceptions (IV, 7 to 17), of which one (IV, 8) was a miscarriage, and one (IV, 16) died at 3 months of general tubercle; the third (IV, 9), aged 21 (1908), is very rheumatic, and when ill very hysterical; the first, eighth, and ninth (IV, 7, 14, 15), aged 22, 11, and 9, are night-blind with retinitis pigmentosa of a somewhat atypical form; IV, 7, seen by Dr. Maude in 1894 (aged 8), and again in 1896, had V. 6/18, with some compound H. As. (II. 1 D. and

* A Case of Ophthalmoplegia with Graves's Disease, Brain, vol. xv, p. 121 (1892): and St. Bartholomew's Hospital Reports, vol. xxvii, p. 137 (1891).

2·5 D.), characteristic stellate pigment collections in retina towards periphery and stippled patches less peripherally, thinning of choroid, especially about y.s. (drawing made at this time); saw Mr. Gunn at Moorfields about March, 1896, who noted "Retinitis pigmentosa, with secondary optic nerve atrophy and highly contracted Fs."; in 1906 was still able to earn his living; is now (1908) æt. 22. IV, 14, seen by Dr. Maude in 1906, aged 9, and examined again in more detail by Dr. Amy Sheppard, Ophthalmic Surgeon to the New Hospital for Women, in April, 1908 (aged 11); probably no change between the two dates; V. 6/24 with each, choroids markedly thin, discs pale, retinal arteries narrowed; dotted patches of pigment and some definite lines of pigment following the vessels, at equatorial region; central region fairly normal. IV, 15, two years younger than IV, 14, V. 6/36, slight H.; ophthalmoscopic changes similar to those in elder sister, but rather less extensive and discs less atrophic. IV, 12, aged 12 or 13, examined at same time (April, 1908), and found to have quite normal fundus and refraction slightly H. The affected girls, IV, 14 and 15, have grey or dark grey irides and somewhat fair complexion, but the choroids are paler than would be expected with such complexions, and cannot be considered normal. IV, 17, living, æt. 3 (1908), has not been examined.

Fig. 83 h



CASE 831.—The patient's father had retinitis pigmentosa, his mother suffers from dead fingers, and a sister is a martyr to chilblains.

Mr. ——— (P. 56, 49) seems to have had no noticeable night-blindness till he was about 32, when, although Fs. were full, V. 5/5 and refraction normal, the retinal arteries were slightly too small and O.Ds. palish and blurred, but no pigment changes anywhere; two years later V. had sunk to 5/12, arteries smaller, still no visible pigmentation of retina, but the pigment epithelium stippled and choroidal vessels decidedly sclerosed. His father, who died of enteric fever at 57, had been blind at night for many years, but could see tolerably by day up to the time of his death; his wife (patient's mother) suffered badly from "dead fingers." She and her husband were not consanguineous; no other cases of the disease and no other degeneracies known. A sister of the patient suffers from very severe chilblains. Patient is fifth of six, all born in nine years, and five living; No. 4, ♂, died at 7 of enteric fever; Nos. 1 and 2 ♀, 3, 4, 5, 6 ♂. Father aged 28, mother 27, at marriage.

In Fig. 104, the old woman with advanced retinitis pigmentosa (III, 5D.) lost the ends of all her fingers from dry senile gangrene when she was about 70 years old.

"Short-sight," probably myopia, is mentioned as prevalent in several of the families; but here, as in the case of tubercle referred to below, the incidence may be the normal one, or merely accidental. Ransohoff's case (Fig. 11, p. 15) may be mentioned; and also that of a boy, Coles (in-patient at St. Thomas's Hospital in 1891), of whom it is stated that there had been much short sight (but no blindness), and much consumption, on the father's side; the boy, aged 12, was the eldest of five. Nos. 3 and 4 died of "fits" under 3, and No. 5 had hip disease. No consanguinity.

Glaucoma is now well known as a not very rare complication of advanced retinitis pigmentosa. The recorded cases were collected by E. Weiss in 1903 and F. Schmidhauser in 1904:—

Case 84 (Blessig) is one of the most remarkable; a husband and wife, not consanguineous, themselves retaining good sight till old age, and with no known history of eye-disease in their descendants, had nine children, of whom none died under 30; the list is as follows:—1. ♀, aged 78 in 1900, chronic glaucoma. 2. ♂, retinitis pigmentosa and deafness, died at 73 in 1897. 3. ♀, normal, died at 73. 4. ♀, normal, died at 68. 5. ♀, chronic glaucoma and deafness, died at 60. 6. ♂, retinitis pigmentosa, died at 54. 7. ♀, normal, died at 64. 8. ♂, normal, died at 30. 9. ♀, retinitis pigmentosa and deafness, died at 55. It is noteworthy that on the whole the elder children lived longer than the younger. Many of them had children who were well known, and were believed to be all normal.

There is often a history of tubercle in the families in which retinitis pigmentosa occurs, but perhaps this association is due only to the normal frequency of tubercle. The number of families—only about 10—in which I find any useful details of tubercle recorded is far too small to be relied upon.

What may be the frequency of the degeneracies and congenital defects associated with retinitis pigmentosa, in comparison with their frequency in families free from that disease, there is at present no means of deciding. Asylums for idiots and deaf-mutes, for instance, probably discourage candidates with defective sight, and such selection, doubtless, accounts to a considerable, though unknown, extent for the comparative rarity of retinitis pigmentosa in Institutions devoted to the care of the deaf and dumb such as is shown by the following often quoted figures:—Liebreich (1861), amongst 241 deaf-mutes in Berlin, found 14 with retinitis pigmentosa: Hocquard (1875), amongst 200 deaf-mutes in Paris, found 5 with retinitis pigmentosa: Brochard (1862), amongst 61 deaf-mutes, found 1 with retinitis pigmentosa; Badal (1881), amongst 200 female deaf-mutes, found 7 with retinitis pigmentosa; Lee (1883), amongst 110 female deaf-mutes, found 6 with retinitis pigmentosa; Sambuc (1896), amongst 33 deaf-mutes, with consanguineous parentage, found 5 with retinitis pigmentosa;

Mulder (1902), amongst 383 deaf-mutes, found 11 with retinitis pigmentosa; amongst the total 1228 deaf-mutes, 49, or about 4 per cent., with retinitis pigmentosa.

Such complications or equivalents were present in one or more members of at least 30 of my own series of about 120 unselected families containing retinitis pigmentosa; allowing for defective note-taking and untrustworthy statements, we may say one-third without exceeding the true limit. In 20 of these 30 families some of the complications occurred in persons not themselves affected by retinitis pigmentosa: in 10 of these 20 families those who had retinitis pigmentosa had also one or other complication, and in the 10 others the complication occurred only in the subjects of the eye disease. Thus in 20 of the 30 families where complications were recorded one or more persons suffered from the retinitis and from some complication as well. The number of persons affected by both retinitis pigmentosa and deafness in the 270—280 with retinitis pigmentosa in my 120 families was 9, or about 3·3 per cent.

The above very incomplete data show that at least 3·3 per cent. of persons with retinitis pigmentosa may be deaf, and at least 4 per cent. of deaf-mutes may have retinitis pigmentosa.

Much more important than such fragmentary statistics is the observation that certain stocks of retinitis pigmentosa are quite free from any of the complications. Indeed, all the most extensive pedigrees of the disease show this immunity from other degeneracies of the nervous system, deafness, idiocy, and the like, and it is doubtless this strict limitation of the inheritance to a character or an organ not of vital importance that enables the family to survive.

This paper would be incomplete without further reference to certain *variations of the clinical characters and pigmentation*, and to the *atypical forms of retinitis pigmentosa*. The position of the latter as a whole has been admirably put by Mr. Hutchinson.* "In some respects," he

* Hutchinson, The Ophthalmic Review, vol. i, p. 26 (1882).

writes, "retinitis pigmentosa stands as an isolated malady in which hereditary descent keeps its type firm, but in other respects probably we shall make a great mistake if we regard it as other than a well-bred member of a family group in which there are other close relatives, and possibly some mongrels"; and, again, there are forms of disease "which deviate from it" (retinitis pigmentosa), "until we may feel doubt as to whether they should be grouped with it or not."

No linear classification of these irregular forms is possible, for we meet with various combinations of departures from the type; but the examples given below illustrate some of the more important of them.

Variations in the Clinical Characters.

Not only does the night-blindness of retinitis pigmentosa begin some years before pigment is visible, and the age at which the typical symptom is first observed vary within wide limits; but in cases examined at a stage which seems from the history to be the same, differences in the apparent quantity and distribution of the pigment and its exact site in relation to visible retinal vessels are often noticed, and similar variations occur in the degree of diffuse retinal haze and disturbance on removal of the pigmented epithelium. The state of vision both as to field and acuity is, I believe, closely associated with the size of the retinal arteries; except that when there are changes at the yellow-spot area, acuity is, of course, disproportionately lowered. The time at which the disease culminates in blindness varies from birth, or early childhood, to advanced old age, and it can hardly be doubted that these very wide limits depend partly on variations in its rapidity, and not entirely on differences in the time of its commencement. These several characters are mentioned in the same paragraph because they cannot be dissociated, although it is not to be supposed that they all vary together in the same degree.

Earliest Visible Changes.—At whatever age the morbid

process begins, the first ophthalmoscopic change seems to be the same—an irregularity in the distribution or appearance of the pigmented epithelium, and soon after this, or perhaps at the same time, minute pale dots or spots appear amongst or between the pigment cells. The result is a general dappling or mottling, which varies in character with the amount of change in the epithelial cells, the clearness of the pale dots, and the degree of pigmentation and vascularity of the underlying choroid. Such terms as "granular," "punctate," "dotted," "stippling," "irregular thinning" or "disturbance" of choroid, are in use for these appearances. The pale, or white, or yellowish dots are probably the so-called "colloid" bodies on the membrane of Bruch formed by deposit from the pigment epithelium*; at later stages they may become inconspicuous either because they run together or get covered by pigment in the retina. These early changes are commonly limited to the periphery or equator, but in atypical cases they are seen also at the central area. The characteristic subsequent pigmentation of the retina seldom, however, affects the central region, even when the early changes have occurred there, and if the examination of a case showing central changes were confined to the y.s. area the true nature of the disease might be overlooked. The prepigment changes may be seen in adolescents or young adults whose symptoms are recent, *cf.* Case 831, above; but I think observations are still wanted of their occurrence for the first time in middle life, though we should expect them at such period if retinitis pigmentosa does sometimes set in so late as the clinical history of some of the senile cases seems to indicate.

Case 85.—Mr. ——— (P. 19, 2) began to see badly at night when about 13; at 16 (1889) I found mottled epithelial changes at periphery, some haze of retina, early typical change of O.Ds. and retinal vessels, and a very few visible pigment deposits; at 18, several veins were coated by pigment, and there were other

* Coats, these Reports, vol. xvi, p. 164 (1905).

branched pigment deposits; at 21 pigmentation much more abundant, retinal vessels much smaller; V. still 6/6 barely. A brother, two years older, showed, when 23, the same changes.

CASE 86.—Miss C. (P. 21, 54); night-blindness at about 18; at 20 (1890), irregular disturbance of peripheral epithelium, innumerable small pale spots, some atypical pigmentation, and at central region considerable retinal haze; O.Ds. palish, retinal vessels about normal; V. 6/9; Fs. much contracted; at 25, characteristic stellate pigmentation.

In Fig. 18 (p. 19), III, 1 and 2 showed no night-blindness till æt. 18 and 24 respectively; when seen at 29 and 27 complexion and choroids fair, but in spite of contracted Fs. and night-blindness with V. 6/9 there was merely peripheral disturbance of epithelium and no visible pigmentation of retinæ; retinal vessels normal; *i.e.*, the morbid process had made but little progress in several years.

CASE 87.—(Peltesohn); ♂, failure of sight began at 19. At æt. 21, V. – 2D., V. 6/6 nearly; Fs. good in daylight, reduced to 10 in dull light; retinal arteries somewhat contracted; small, bright, distinctly defined spots at periphery; no trace of pigmentation; æt. 25, characteristic pigmentation of retina, bright dots present, but now for most part pigmented.

The *seat* of the earliest pathological changes of retinitis pigmentosa has been briefly considered at p. 151, but reference should also be made to the recent work of Stock.* From microscopical examination of an eye with typical retinitis pigmentosa, excised during life in an operation for adjacent carcinoma, and fixed immediately in Zenker's fluid, Stock concludes that the bacillary layer is the first structure to suffer, the choroid and the pigment epithelium being affected only in a secondary manner. The field of vision in this patient was reduced to about 5°,

* Stock (W.), Über eine besondere Form der familiären Amaurotischen Idiotie, Bericht der ophth. Gesellschaft, Heidelberg, 1906 (published 1907), p. 48. The same cases are described more fully and illustrated by microscopical drawings under a similar title in Klinische Monätsbl. f. Augenheilkunde, vol. xlvi, p. 226 (March, 1908).

and corresponding to this the rods and cones at the macular region itself were intact, but they disappeared a very short distance from the macula. Similar primary disappearance of rods and cones was found in the eyes of three children with an atypical form of retinitis pigmentosa and complete blindness associated with mental failure; both conditions came on during about the sixth year of life, and were probably due to hereditary syphilis, the father having had the disease between the birth of his first born, who remained healthy, and the second; those affected were the second, third, and fourth, and all of them died of phthisis before puberty. The ganglion-cell layer showed some, but not very profound, changes; the nerve-fibre layer almost normal, and the optic nerve not atrophied. During life there was some narrowing of retinal arteries, some pallor of discs and remains of previous iritis in two of the three, but not all of these appearances were present in the same two children. The remarkable clinical phenomenon was the complete blindness with what appeared to be insufficient ophthalmoscopic changes, a condition explained by the entire destruction of the rods and cones.

Stock's description may be compared with the account by Lister* of the retina and choroid in a man who had been blind for some years from advanced typical retinitis pigmentosa; the rods and cones were altogether absent, but at the macular region the pigment epithelium still formed a well-marked layer, and in the same region the ganglion-cell layer was still well seen; the choroid was atrophied (as would be expected at such a late stage of the disease), but the choroidal vessels seen in the sections showed no thickening of their walls.

The *earliest age of visible pigmentation* is illustrated by the following cases:—

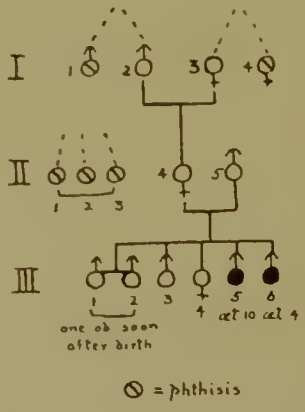
Case 88.—Gertrude Lewis. Typical abundant pigmentation, at æt. 6 years; said to have had bad sight, especially by

* Lister (W. T.), A Case of Retinitis Pigmentosa with Pathological Report, these Reports, vol. xv, p. 254 (1903).

dull light, from earliest infancy, and presence of nystagmus supported this history; refraction H. 5 D.; Fair hair, hazel eyes. Mother and father both fair. She counted fingers at 5 m. and would perhaps have done better had she known her letters.

Case and Fig. 89.—Dr. E. J. Smyth, of Guildford, sent me in 1906 notes of a childship of six (D. family) in which three of the first four (3 ♂, 1 ♀) are living and have perfect sight (one, a twin, died soon after birth); the 5th (III, 5) (♂), aged 10, was noticed to be night-blind when 2 years old and at 10 had typical retinitis pigmentosa; the 6th was night-blind when barely 3 and at the age of 4 had a few patches of pigment at the periphery of each fundus and the retinal arteries somewhat shrunken; no consanguinity or history of other cases; parents living and have good eyes; phthisis in mother's maternal aunt (I, 4,), three of mother's paternal cousins (II, 1, 2, 3), and in her paternal uncle (I, 1).

Fig 89



In the patient V, 39 of Case 1, in this paper (p. 9), some characteristic pigment was seen at the age of 5.

Case 90.—A boy (Frank Barney), æt. 8 (1884) (St. Thomas's Hospital); very copious typical pigmentation all over periphery of each eye, with removal of subjacent epithelium, slightly diminished vessels and a little haze of O.Ds.; night-blindness well marked for a year (probably longer), V. 20/100 and 1 J., Fs.

contracted to 20°—30°. It may be specially noted that this child, though showing so much retinal pigmentation, had fair hair.

CASE 91.—Mooren (5, 1882) saw June 3, 1868, a boy, aged 3, with pigment in the retina; seen again at 6, the pigmentation did not seem to have increased, but the night-blindness was worse; several maternal cousins were night-blind.

CASE 92.—Cant (1886); a childship of four, aged from 15 to to 5, in which every one had the disease; in the youngest (aged 5) the periphery was dotted with minute spots of pigment; in the eldest the pigment was much more abundant; no known history of bad sight in family, no consanguinity; father epileptic.

CASE 93.—Risley (1886); "absorption of pigment" in a child aged 2 years; in an older sibling some "absorption of pigment" with deposits at between 3 and 4 years of age, and a year later, say æt. 4½, pigment spots at periphery.

CASE 94.—Hasket Derby (same reference as Risley); boy noticed to see badly in the evening when between 1 and 2 years old; examined, not very thoroughly, at 3, and no disease seen, but at 8 typical retinitis pigmentosa, as had his sister, then aged 7. No family history of the disease and no consanguinity of parents.

CASE 95.—A boy (Rowland), æt. 8 (1887) (St. Thomas's Hospital); for two years or more had had "to feel about for his food" and shown bad sight in other ways; epithelial disturbance at y.s. and equator; V. only 3/60 and letters of 16 J.; refraction low, mixed As.; pigment ensheathing some of the large retinal veins for a long distance, O.Ds. rather pale and arteries rather narrowed. Æt. 14 (1893), thought to be worse; y.s. regions as before and in L. several blots of brownish pigment; zone of classical pigmentation between central region and equator, many large veins sheathed in pigment.

CASE 96.—Höring (junr.) (1864) saw fine bright points and streaks in choroid and very slight pigment deposits in retina and shrinking of retinal arteries in a boy of 5.

Case 97.—Coleman (1889), Case 4, boy aged 4 8/12, very intelligent; nystagmus and bad V.; "dots" of pigment and white dots scattered over the retinæ; defect of sight noticed by parents when he was 9 months old; elder brother, aged 8, blind from infancy and can hardly tell light, no ophthalmoscopic note; sister, aged 18 months, seems to see well. Parents doubly consanguineous, their fathers being first cousins and one of them (patient's mother's father) first cousin to his wife.

Schneider (Fig. 3, p. 12) V, 4, a well-developed boy, 3 years old, had strongly-marked night-blindness with peripheral pigmentation of retinæ, O.Ds. pale and retinal vessels showing some shrinkage.

Case 98.—Hirschberg (4, 1874), ♂, aged 15 months, born blind and now no p.l., intelligent and well developed; fundus thickly sprinkled with black points, especially towards periphery, O.Ds. reddish and slightly hazy; is third born; Nos. 1 and 2 normal. Parents married seven years and are first cousins (patient's mother's father and father's mother were sibs.).

The above cases show that slight though characteristic deposits of pigment may be ophthalmoscopically visible in the inner retinal layers certainly at from three to six years of age and probably as early as 15 months; and that the changes may be quite advanced at 7 or 8.

The cases described by Leber as *Congenital Retinal Atrophy*, in which the disease probably begins before birth, though not genetically distinct from the above, will for convenience be referred to later under *retinitis pigmentosa sine pigmento*.

The regional distribution of the pigment may be more or less peripheral or equatorial and may form a complete or a broken belt. Marked differences are also seen in different patients in the size of the individual "bone corpuscle" deposits, lines, or radiating figures, and in the area of the meshes or spaces enclosed by them, such variations being conditioned largely by the grade of the vessels—capillaries, venules or larger veins, in the walls of which the pigment has been arrested. When the vessels so ensheathed are large enough

to be seen, careful observation shows that they are invariably veins; in spite of much careful search, I have never (unless in a drawing) seen an artery with pigmented coats; the pigment always travels in the direction of the blood-current. That in some cases the pigment reaches the larger veins comparatively soon and in quantity, whilst in others it stays longer in the neighbourhood of the venous radicles, may possibly be explained by individual differences in the perivascular lymph spaces, such as we are led to expect from a study of certain other retinal diseases, for example embolism and renal retinitis. It seems possible that free and early passage of the pigment to the visible veins may leave the capillaries relatively free and the arterial current good; and it may be noted that these conditions were present in several of the patients in Fig. 104, viz., III, 18, aged 55; IV, 6, 44; and IV, 12, 28. Considerable variations are also seen in the degree and extent of diffuse retinal haze, and these do not depend either upon the stage that the disease has reached or upon differences in the colour of the choroidal background.

It might be expected that the *quantity of pigment in the retina would be related to the complexion*, *i.e.*, general pigmentation, of the individual or at least to that of his choroid; but as the pigmentation of the hexagonal epithelium is probably about the same in all normal eyes, the expectation would not be justified. The point has not received much attention since Leber alluded to it many years ago; it is difficult to decide clinically. There is no doubt, however, that abundant and perfectly typical pigmentation is met with in persons of fair complexion as well as in those who are dark. Thus in Case 104, compare IV, 12, and IV, 6; the former, aged 28, has very fair hair, white skin, quite blue irides and fair choroids, but abundant pigment deposits of typical bone-corpuscle type forming a complete zone in each eye and some of it lying in the sheaths of large veins; she has had some difficulty in the dusk from her earliest recollection; V. now 6/9 with each

eye, and in spite of the quantity of coarse pigmentation, and the marked disturbance of epithelium in the corresponding parts, the retinal arteries are but slightly shrunken and might have been passed as normal in a cursory examination (1907). Her cousin (IV, 6), aged 44, with dark hair and brownish irides, has exactly similar coarse pigmentation. In these two, one very blond and the other decidedly dark, the quantity of pigment in the retina is practically alike when allowance is made for the 16 years' difference of age. Other illustrations are seen in Cases 88 and 90 above. Snell (1, 1886) saw retinitis pigmentosa in six brothers, aged from 14 to 25, the pigment increasing with age from youngest to oldest; but all were blond, with hair from fair to light brown. Other cases are:—

Case 99.—(P. 7, 43); moderate pigmentation with fair choroids and sandy hair in a man of 55; had been night-blind as long as he could remember anything and used to knock against obstacles when he was a boy; V. 6/18 and 1 J.; retinal arteries moderately shrunken.

Case 100.—(P. 44, 163); a lady of 39 with reddish brown hair but fair choroids; equatorial belt densely pigmented; had "always" seen badly in the dusk, but still had V. 6/18, and with correction of slight M. As. 6/9 and fairly good Fs.

In the following cases the choroid was dark; the disease was of long standing in both.

Case 101.—Woman, 54 (Hilyard, M.O.P., 1, p. 13, 1883); bad sight with night-blindness "all her life"; typical retinitis pigmentosa with small arteries, atrophied O.Ds., sclerosed choroidal vessels and removal of pigment epithelium; "although the choroids are very dark the amount of pigment in the retina is comparatively small."

Case 102.—Dark hair with much pigment in retina (P. 41, 223); man, 48, with black hair; V. reduced to fingers at 0·5 m., scarcely any F. and the history that he had been night-blind since boyhood; excessive pigmentation of retina with extreme shrinking of retinal arteries and pale, hazy discs.

Making due allowance for want of uniformity in the descriptions, even when made by the same observer, I think we may conclude from the above cases, and others that could be given, that the apparent quantity of pigment in the retina in this disease is not correlated with the complexion of the patient's choroid, hair, or skin.

The age at which blindness becomes complete varies within wide limits, even if we omit the rare cases (Leber and others) when the child is blind at birth or in early childhood. Soelberg Wells in his admirable summary* of the malady gives from 35 to 50; Liebreich,† 30 to 40; De Wecker,‡ 45 to 50; Schmidt-Rimpler,§ about 50; Schöbl, in Norris and Oliver, III, p. 467, 50; Fuchs,‖ the sixth decade or later; Parsons¶ gives 60 or later as the usual period at which central vision is lost.

Although many may keep a remnant of sight till quite old age, useful vision is lost between about 30 and 45 in a large number. Occasionally, however, persons with advanced typical retinitis pigmentosa, aged from 50 to 70, retain central V. of 6/24 to 6/9, and give a history, which we have every reason to accept, that no failure of sight was felt till well past middle life. Such cases are spoken of as *senile retinitis pigmentosa*, but we do not know whether they illustrate late commencement of the disease or only very slow progress; and the decision is rendered more difficult by the well authenticated occurrence, at all ages, of cases where the classical symptom of *night-blindness* was either *absent or unnoticed*, or perhaps sometimes concealed, even when the retinal changes were strongly marked. For example:—

Case 103.—Marlow (1894); ♀, 20, V. 6/9 to 6/6 and 1 J. easily in both bad and good light, but with the Fs. contracted

* Soelberg Wells, Treatise, etc., 2nd Edition, p. 372 (1870).

† Liebreich, Atlas, Tafel VI (1863).

‡ De Wecker and Jaeger's Traité and Hand-Atlas, p. 143 (1870).

§ Schmidt-Rimpler, Augenheilkunde u. Ophthalmoscopie, 6th Edition, p. 275 (1894).

‖ Fuchs, Text-book. Amer. Trans. of 11th German Edition, p. 489 (1908).

¶ Parsons, Diseases of the Eye, p. 365 (1907).

down to 5°—7·5° (tubular vision) and typical pigmentation of retinæ up to within three disc breadths of O.D. In walking she always kept her eyes on the ground to avoid stumbling, but neither now nor at any time had she had any greater difficulty in the dusk than in daylight. Her sight had been thus from her earliest recollection, but was believed to be getting slowly worse. No note as to whether she had a belt of extreme peripheral vision, nor as to size of retinal vessels.

In Hutchinson's case, mentioned at p. 156, there had never been any particular difficulty at night. In another case by the same author (these Reports vi, 222), in a man of 60, and in a brother and sister aged 16 and 17 mentioned by Aneke (his cases 1 and 2), the same feature is emphasised.

This state of things is intelligible where the periphery of the retina is still tolerably healthy (ring scotoma with a wide belt of peripheral vision).

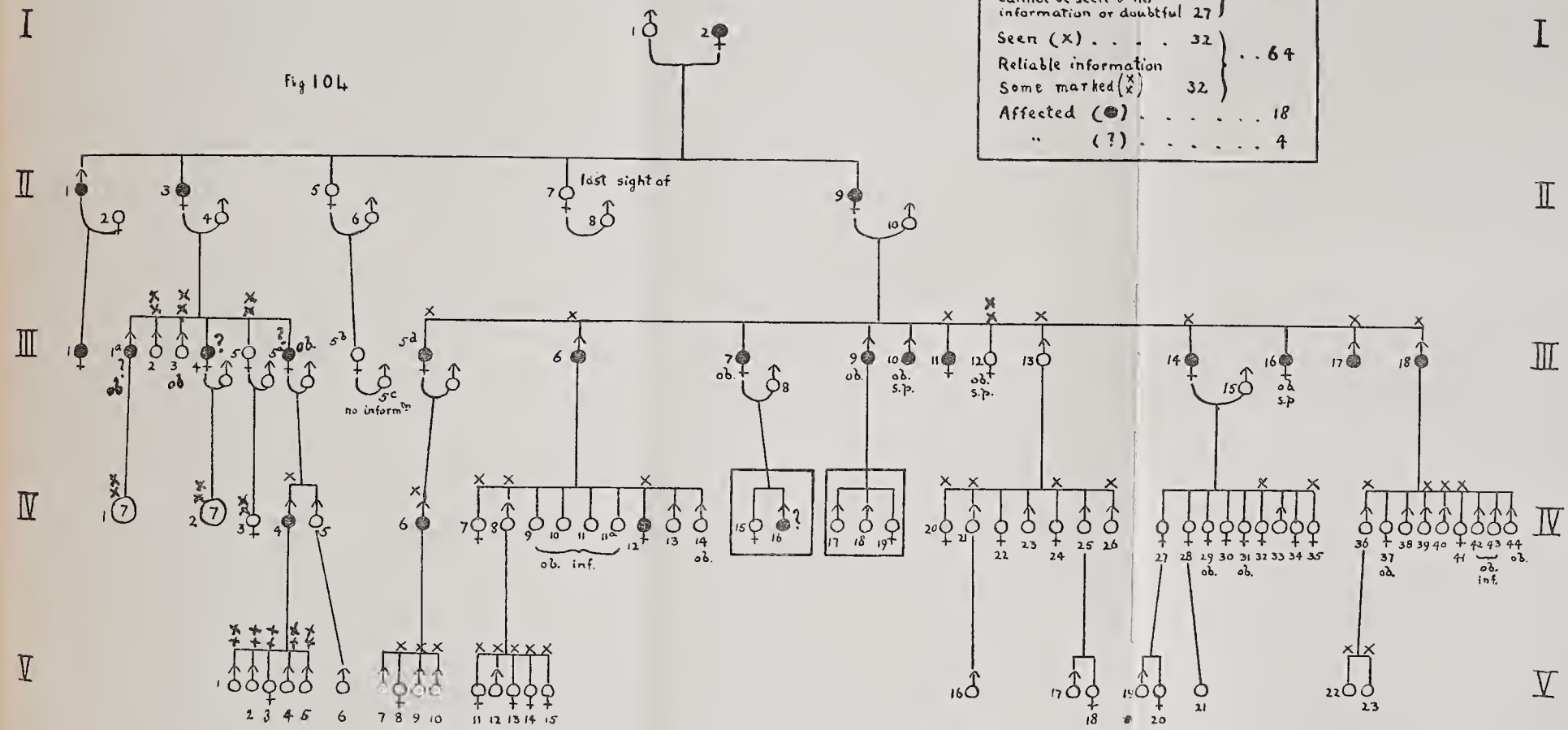
It was well marked in Case and Fig. 104,* IV, 6 (already quoted in connection with complexion); he was an intelligent man of 44, of out-door habits, accustomed both to country and town life, with very good central acuity separated from a broad belt of peripheral vision by an incomplete ring scotoma which became much larger in a subdued light; he said he never had difficulty at night, but a relation afterwards told me she had thought for many years that he had some degree of the family blindness; the fact is that he had learned to compensate. His disease, though severe as regards pigmentation of the retina, had not led to much interference with arterial supply. His mother (III, 5 *d*), aged 78, told me, quite independently, that she had never had difficulty in going about at night; she has advanced retinitis pigmentosa with some haze of lenses, but says she could see to read till "2 or 3" years ago; has lost several fingers of both hands from senile gangrene within the last year.

* Part of this case has been given already as Fig. 6 at p. 13. One of the family recently came under the notice of Mr. Treacher Collins at Moorfields, whose clinical assistant, Major P. P. Kilkelly, M.B., worked out a large part of the pedigree for me, and I have since seen a large number of the other members myself.

(*To face p.* 360.)

Retinitis Pigmentosa

Fig 104



Total (Gens. I to V)		104
Dead & nothing Known	13	40
Cannot be seen & no information or doubtful	27	
Seen (X)	32	64
Reliable information		
Some marked (X) (X)	32	
Affected (●)		18
" (?)		4

In this large family, late completion or very slow progress has been the rule, just as relatively rapid progress or early onset is noticeable in others.

Additional cases illustrating either late onset, or early commencement with extremely slow progress, are:—

Case 105.—George Taylor, 59 (Moorfields, June, 1884). H. m. 5 D., V. corrected 20/70; said his sight had been good, except the need for glasses, till he was 52, when he began to see badly at night; advanced typical changes with very pale O.Ds. and very shrunken vessels.

Case 106.—Wm. Jeffrey, 63 (Moorfields, August, 1897). My. 2·5 D., V. corrected 6/24; sight very good both day and night till five or six years ago, now worse in dusk. F. of R. much contracted, L. less so; typical pigmentation of periphery in each, O.Ds. blurred, reddish grey, retinal arteries decidedly narrowed. His sister, 61, seen on same day, had normal V. with slight H. corrected; at inner part of R. fundus an area showing stellate arrangement of pigment, but nothing of same kind in L.; crescent of choroidal atrophy on temporal side of each O.D.

Case 107.—John Stephens, 72, St. Thomas's Hospital, March, 1882. Labourer, rather deaf. Married 36 years. Wife states that he had no difficulty in seeing at night until five or six years ago; worse the last year and a-half. Always short-sighted; V. now with My. 5 D., corrected 20/40 partly; changes typical.

Case 108.—A Jew (male), aged about 70, at Moorfields, October 30, 1885 (P. 12, 23), nearly blind from loss of Fs. with severe typical changes, stated that he never had the slightest defect of sight either by night or day till he was about 50.

Case 109.—A clergyman, æt. 68 (P. 37, 116), came in February, 1896, about spectacles, having no idea that he had any disease; V. 6/9 with each eye, slightly improved by − 0·5 D., and with + 3 D. read 1 J. Abundant retinitis pigmentosa around the entire periphery in each eye with two or three circular patches of atrophy of chorio-capillaris; O.Ds. a little

pale and hazy, but retinal arteries of good size; a small opacity to nasal side of posterior pole of R. lens. No night-blindness whatever. Fs. not measured.

CASE 110.—Kanpp (Case 2) (1890); a man, aged 66, almost blind from advanced retinitis pigmentosa, said V. had not begun to fail till he was 50.

CASE 111.—Darier (Case 3) (1887); three brothers, Nos. 3, 4, and 5 in childship of 5, have retinitis pigmentosa. One of them, now 77, fundus still visible, showing typical changes; night-blind from childhood, but could see to do his work (blacksmith) till æt. 67, when he was disabled, not by the retinitis, but by senile cataract; another affected brother died, still able to work, at æt. 77; third affected brother, also a smith, continued his work till death, æt. 46. The children and grandchildren of first case known to be free.

Such cases as the above, occurring in different social classes, do not support De Wecker's* contention that the course of the disease is retarded by conditions unfavourable to good health.

A few cases of *retinitis pigmentosa* have been *complicated with day-blindness* or dislike of bright light *with colour-blindness*: Knapp (1870); Reinecke (1894); Coroenne (1887), and one of my own (Fig. 68, p. 45).† It is not clear that these cases form a homogeneous group.

Ring scotoma, although known almost from the beginning,‡ was for a long time looked upon as exceptional, if we may judge by the slight attention given to it in many of the systematic books. For many years I have had numerous charts showing ring scotoma in cases of my own. According to Hepburn,§ it is almost universally present. It is likely to escape detection unless sought for. We can hardly doubt that variations in the symptoms, especially in the

* De Wecker and Landolt's Traité complet, IV, 135.
† St. Thomas's Hospital Reports, vol. x (1880).
‡ Von Graefe, A. f. O., vol. iv, 2, 250 (1858).
§ Hepburn (M. L.), these Reports, vol. xvii, p. 232 (January, 1908).

apparent size of the field and the degree of night-blindness, must depend a good deal upon the form, position, and dimensions of this peri-central, annular, or ring-scotoma, *i.e.*, upon the amount of the periphery remaining intact.

Variations in the Ophthalmoscopic Changes.

Retinitis pigmentosa with central changes is not very uncommon. Cases have already been given in connection with some of the exanthemata (Cases 80 *et seq.*). In others no such illness is recorded. The change at the posterior pole usually occurs as an area of disturbance or removal of pigment epithelium with some scattered black dots. This may take the form of an island with sharp though irregular outline; or it may show no clear boundary but merge into apparently normal structure, which again may be succeeded more anteriorly by a belt of typically pigmented retina; or the epithelial disturbance and subjacent choroidal sclerosis may occupy a large part of the fundus, with little or no typical bone-corpuscle pigment. The O.Ds. and retinal arteries are altered as in ordinary cases, but sometimes in only a slight degree. Central vision is much damaged, and the patients instead of being night-blind often prefer a rather dull light. The morbid process seems often to have begun in early life, and is perhaps sometimes congenital.

Case 112.—Amongst published cases of this central variety, Case 9 in Leber's paper (2), 1871, was probably an example, though the area of central disease at y.s. involved the choroidal stroma as well, whilst the rest of the fundus showed similar change limited to the epithelium. The boy was 15 when seen, and had V. = fingers; his sight had been in the same state, as far as could be ascertained, since soon after birth, and had prevented his learning to read. Parents first cousins. In the same paper Leber gives other cases with predominant failure of central vision, but the appearances of common retinitis pigmentosa only, and history of onset several years after birth.

It was perhaps to cases resembling Leber's that De Wecker referred, in 1868, when he divided retinitis pigmentosa into two

groups:—One, in children, in whom predominant lowering of central vision and comparatively quick progress were frequently associated with mental defects;* the other, the ordinary cases, beginning with night-blindness early in life, progressing very slowly and usually not associated with mental failure.

Case 113.—Hirschberg (1, 1889); man, aged 21, who had seen badly at night for three years, now V. 15/20, Fs. full in day, but contracted in dim light. Media clear; typical peripheral pigmentation, but, in addition, whole fundus thickly sprinkled with minute black dots, each placed at the centre of a whitish spot;† (a black and white illustration is given); O.D. yellowish and hazy; retinal vessels not mentioned, but represented as of good size. No other cases known in the family. Parents not consanguineous.

Case 114.—Knapp (1870); a lady, aged 35, dated slow failure of sight from 10 years back; the ordinary pigmentation had invaded the y.s., the intervening retina between the spots in that region being whitish and opaque; there were also white specks scattered amongst the black ones in all parts; O.Ds. and retinal vessels not described. Up-out quadrant of each fundus free from pigment and "perfectly normal"; F. not contracted, but a large central scotoma; night-blindness not well marked. No consanguinity.

Case 115.—Dor (2, 1883); brother and sister; the brother, seen at 21 (1881), dated his night-blindness from severe small-pox when æt. 4 or 5 years; scars still present; is deaf; V. in daylight 20/30, in dusk 20/100; colour V. normal; F. considerably contracted in dull light; no pigmentation of fundus, but diffuse whitish-grey opacity of retina, obscuring the choroid, from posterior pole of eye to equator; in front of equator it gradually breaks up into scattered greyish dots; retinal vessels normal; the opacity obscures the y.s. The sister (older

* Compare with the cases by Stock, *supra*.

† This appearance, innumerable, rather small, pale spots, each with a single, much smaller, black dot at its centre, is characteristic of one variety of chronic choroido-retinal degeneration, and has no doubt often been observed. I find it described in the notes of several of my own cases. Hirschberg's illustration is particularly good.

than he) not seen, but has similar failure, also dated from small-pox, which she contracted at same time as brother.

Retinitis pigmentosa sine pigmento usually signifies nothing more than the initial stage of the ordinary disease. The want of pigment is to a large extent apparent only, for pigment in small grains, confined to the outermost layers of the retina, may be invisible in ophthalmoscopic examination, and will certainly be so if the retina be intransparent, as it often is during the earlier period of the disease. This was the state of things in the case described and examined by Perrin and Poncet, and quoted at p. 151 above. In time, usually a few years, the pigment travels into the inner layers, and then becomes visible either in the "bone-corpuscle" or "spider" pattern, or as lines following the retinal veins, never the arteries. Thus almost every case of retinitis pigmentosa may be described as "sine pigmento," if seen early enough. This is true at whatever age it commences, whether before birth, as in the rare condition described by Leber (1, 1869) and others* as congenital retinal atrophy, and regarded by him as retinitis pigmentosa that had run its course during fœtal life, the pigment not becoming visible till one or more years after birth†; or in childhood, youth, or early adult age. But it would seem that now and then an advanced degree of atrophy of the pigment epithelium and its consequences may be reached without subsequent migration of the pigment into the retina, the condition named by Leber retinal sclerosis without pigmentation.‡ The condition must be rare; the following are examples:—

* Mooren and von Graefe appear to have recognised such cases before Leber wrote about them. Two cases published by Hutchinson, in 1866, may have been of the same nature; the patients were sisters, aged 4 and 1½ years. (These Reports, vol. v, p. 347.)

† Cases of excessive pigmentation of retina in young adults said to have been born blind are mentioned by Knapp (1870), Harlan (1885—86) and Ficuzal, and in a boy of seven by Simi (1866).

‡ Leber, Graefe u. Saemisch, vol. v, p. 641 (1875—77).

Case 116.—Alvarado (1882); ♂, 32, nystagmus and sight failing from childhood; very careful examination showed no trace of retinal pigmentation, but the epithelium was removed (or bleached), retinal arteries small and O.Ds. pale.

Case 116A.—Derigs (1882) (author's Case XII); ♀, 36, with very abundant retinal pigmentation; lenses clear; V. 20/70, F. contracted to from 10°—20°. (Case XIV), ♂, 32, brother of last, R. My. 1/30, L.H.As., Fs. contracted to 30°—40°, night-blind, "ophthalmoscopic appearances entirely negative." (Case XIII), ♀, 24, sister of the two last, V. 20/40, Fs. contracted to 25°—50°; retinal pigmentation "not quite so strongly marked as in the elder sister." Another brother affected, but no particulars. Parents consanguineous. This case is important as showing the common pigmented form and the rare unpigmented variety in members of the same childship; XIV would be more valuable if the condition of O.D. and retinal vessels had been fully described.

Case 117.—Bruner (1898); ♀, 37, night-blindness for many years, probably getting worse; disturbance and absorption of pigment epithelium at periphery was the only morbid change, retinal vessels normal.

Case 118.—Nolte (1896); ♂, 22, epileptic and stupid, but otherwise of normal development; diffuse atrophy of pigment epithelium causing finely granular appearance, retina rather grey and its vessels much shrunken, choroidal vessels sclerosed; O.Ds. pale. Had been seen in 1886 (æt. 12), with O.Ds. pale and "waxy," retinal vessels very small, fundus normally red, but with a peculiar marbled appearance. Sight had begun to fail at three years old after a severe illness lasting many weeks, with brain-symptoms and diarrhœa. He was third born of eight; fourth, ♀, about a year younger, and eighth, ♂, 11 years younger, had similar ocular and cerebral conditions, but the ophthalmoscopic notes not so full. Two ♀ cousins, similarly affected. No syphilis.

Case 119.—Miss ——, aged 34 (1890) (P. 22, 13); sight found to be very bad almost immediately after birth, and never "took notice" well; before long showed signs of night-blindness. From 13 to 16 was Sir William Bowman's patient; he confirmed the

night-blindness, found V. = 2 to 4 J. held very close, general thinning of chorio-capillaris and a whitish tint of fundus, especially about y.s., but no pigment in retina. When I saw her at 34, V. was barely 16 J., Fs. very small, fine nystagmus ; My. about 3 D ; diffuse pallor of the whole choroid as if pigment epithelium were wanting, especially marked about y.s., where, however, the choroidal pigmentation was well marked ; but no trace of pigment could be found in retina in any part ; O.Ds. very pale (not waxy), retinal vessels very small. She was the second of six ; the third, ♂, had good sight, but died at 27, "acute lung disease" ; fourth, ♂, epileptic idiot, died at 17 ; first-born, ♀, I examined and found normal, five and six reported normal. No evidence of hereditary syphilis. Parents living (1890). Consanguinity not mentioned.

Case 120.—(Morton and Parsons, O. T., xxiii, 135, 1903.) Hyaline bodies at the optic disc, but in other respects resembled the cases we are describing as to the atrophy of pigment epithelium with very scanty deposits in the retina. The patient, aged 24, was night-blind (age at onset not stated), with history of consanguinity of parents and retinitis pigmentosa in an uncle and sister.

More puzzling is Case 121.*—The subject was an old man, 71, whom I saw in April, 1907, and who was examined again with great care by Mr. Chetwood-Aiken later in the same year. He has been night-blind all his life, sufficiently so to prevent him from driving his own horse and cart after sunset and to cause other inconveniences, unless there was a moon, but the defect was not getting worse. Although a number of his relatives have ordinary retinitis pigmentosa, neither I nor Mr. Chetwood-Aiken could find any trace of retinal pigmentation in either of his eyes ; the O.Ds. were normal or at most slightly pale, and his retinal arteries of good size, probably not at all diminished ; refraction slightly myopic ; lenses clear, except for a few striæ below ; can still read moderately small print and tell the time by his watch easily. Compare Case 116A *supra*.

* Published as a member of a mixed pedigree of Congenital Discoid Cataract and Retinitis pigmentosa in O. T., vol. xxviii, 1908. The case is there given as Generation III, No. 18.

Sometimes this permanently unpigmented or very scantily pigmented disease seems to have set in late in life, and forms a variety of senile retinitis pigmentosa different from the senile cases already given.*

Case 122.—Samuel Craig, labourer (M.O.P. letter, 1888), aged 67 ; for two or three years past had been unable to see at night, and was getting worse. V. R. 6/24 ; L. 6/18 ; Ps. and T. n. Hands and muscles of mouth tremulous, never drinks, and tea makes the shaking worse. Retinal arteries diminished, especially in the R. ; choroidal pattern very plain (removal or bleaching of pigment epithelium) ; choroid around O.D. somewhat pale ; changes rather more pronounced in R. than L. No pigmentation of retinæ. Moderate nearly uniform concentric contraction of each F. No history of syphilis.

Case 123.—Morton (O. T., v, 142, 1885) ; ♂. painter, 55. Night-blindness first noticed about five years ago, and has increased; F. now contracted to about 10°, but V. "quite normal" ; absence of pigment epithelium and chorio-capillaris over whole fundus of both eyes except at y.s. area ; choroidal vessels sclerosed near to O.D. ; some fairly typical but scattered patches of pigment in retina towards periphery (much like those in Jaeger's Fig. 80). O.D. shown in the illustration as brownish waxy, and all retinal vessels much shrunken. No history of syphilis. He has a sister who, as well as her child, has been examined, and the eyes pronounced perfect.

Case 124.—Frost (1, 1889, Author's Case 4) ; ♂, 55, formerly in the Indian Army. Sight began to fail at æt. 35 with night-blindness. The changes are now due to removal of pigment epithelium and chorio-capillaris with sclerosis of choroidal vessels, but only scanty signs of retinal pigmentation : no note of O.D. and retinal vessels.

* Another variation in retinitis pigmentosa, difficult to interpret, may be mentioned here. In most cases of ordinary retinitis pigmentosa the visible pigment in the retina and the visible disturbance or absence of the pigment epithelium at the corresponding parts of the fundus vary *pari passu* ; but in some cases where there is much pigment in the retina the subjacent epithelium appears—to ophthalmoscopic inspection—unaltered. The point has been mentioned by various authors, and may be remembered in connection with Stock's cases already quoted. This appearance may be deceptive and depend upon variations in the pigmentation of the choroid.

Another variety of retinitis pigmentosa has been provisionally separated under the title "*Atrophia gyrata chorioideæ et retinæ*," by Fuchs (1896), who has described and figured the disease as it occurred in three sisters and in a fourth subject, a man, aged 29,* as follows:—

CASE 125.—The three sisters (Fuchs's Cases I, II, III), aged 26, 24, and 21, being the first, second, and fourth born in a childship of 10, had in common progressive night-blindness, limitation of Fs., posterior polar cataract, high myopia (10 to 20 D.) shrinking of retinal vessels, and if we may judge from the illustrations (the point is not mentioned), some atrophy of disc. Also, as the special feature, very extensive choroidal atrophy of unusual character; towards the periphery a broad zone of atrophy, showing at its anterior part many and dense pigment deposits, some round, others branched; surrounding O.D. another less regular zone of complete choroidal atrophy or posterior staphyloma free from pigment; between these two zones a belt of healthy choroid in which are a few separate small islands of atrophy. The diseased areas have sharply cut, lobulated borders, as if formed by the confluence of numerous separate patches. In the most advanced case the healthy "zone" was reduced to a single large patch at the temporal side of the fundus, and in one of the other two the round belt was incomplete, the peripheral and circumpapillary areas having penetrated the healthy belt at one place. The disease appears to have begun in childhood, and progressed steadily; V. with correction, varied from 5/24, to p.l. at 5 m. One of the patients had three children, all boys, with normal vision. The three affected sisters belonged to a childship of 10: three died early; seven lived, four males, aged 23, 20, 16, and 12 years, all with good sight, three females all affected as above. Parents first cousins; no other details.

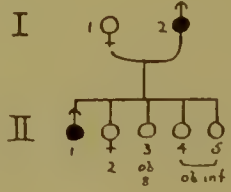
CASE 126.—Fuchs's Case IV; ♂, 29, night-blind from childhood and getting worse; My. 6 D., V. 5/36. Visual Fs. and retinal vessels extremely diminished; an island of healthy

* Described and figured for Professor Fuchs by Coleman W. Cutler in A. of O., vol. xxiv, p. 334, with Plate (1895); from vol. xxx of A. f. A. (1894). Fuchs's own account of the disease based on the three cases from his clinic described as above by Cutler, and an additional case, is found in A. f. A., vol. xxxii, p. 111 (1896).

choroid at y.s., also some normal choroid on the equatorial atrophic belt and at anterior part of that belt, but not of the typical shape; extreme periphery of choroid normal. No consanguinity of parents, and no other cases known in the family.

Case and Fig. 127.—E. Jacobsohn published, under the title of "Retinitis pigmentosa atypica," a case of probably the same disease, with coloured ophthalmoscopic plate. II, 1, ♂, 20, night-blind from very early life; Fs. now very small, V. 20/100, and smallest print at 3 to 5 inches (refraction not noted, but low myopia probable); O.Ds. and retinal vessels as in retinitis pigmentosa; choroid healthy over a large area at posterior pole of eye, including O.D. and y.s.; in front of this normal district

Fig. 127



large areas and patches of the choroid were atrophied, its vessels sclerosed and the overlying retina abundantly pigmented; patient physically weak and feeble-minded, skull very small. Father (I, 2), æt. 48, has a similar condition of fundus; night-blind from earliest life; slow failure; now quite blind for a year and a-half. Mother (I, 1), My. 1·5 to 2 D., V. 20/50 each eye; fundus normal. No consanguinity. Patient is one of five born and two surviving; II, 2, aged 15, normal; II, 3 died at 8 years, and the two others in infancy.

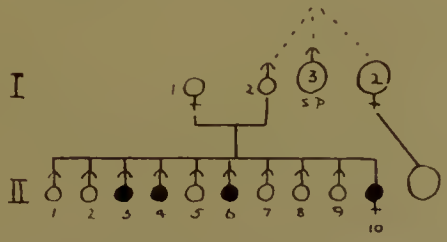
Case 128.—Förster,* in 1857, *i.e.*, soon after the introduction of the ophthalmoscope, described a case of night-blindness dating from early childhood in a girl aged 17; nystagmus, some myopia (amount not given), and amblyopia even by daylight; stroma of choroid almost entirely devoid of pigment and

* Förster, Über Hemeralopie und die Anwendung eines Photometers, p. 42 (1857).

epithelium wanting, but the large vessels present; retina showed no changes; irides blue with brown spots; F. decidedly contracted in the dusk. But for the night-blindness and contraction of F. this case would be more properly classed as albinism affecting the eyes alone. It is possible, however, that it belongs to group we are now considering.

CASE and Fig. 129.—This remarkable case, which evidently bore much resemblance to those of Fuchs just cited, was published by the late Mr. Zachariah Laurence in the old Ophthalmic Review, vol. ii, p. 32 (1866), and again quite independently by Mr. Hutchinson in his Archives of Surgery, vol. xi, p. 118 (1900),* with a coloured ophthalmoscopic plate; it was also referred to briefly by Mr. Hutchinson in his paper on Retinitis pigmentosa in the new Ophthalmic Review (Priestly Smith's), vol. i, p. 28, 1882. The subject of

Fig. 129



Mr. Hutchinson's Plate (Fig. 129, II, 10) was a girl aged 16, when the drawing was made about 1873—74, whose sight began to fail when she was about five or earlier; a narrow zone of choroid immediately around the O.D. appears quite natural; then comes a very broad zone of incomplete atrophy, leaving only the large vessels, and even they are converted into white bands; about the equator the choroid becomes gradually less atrophic, although the pigment epithelium and chorio-capillaris appear to be universally absent; some angular and stellate pigment deposits in the retina, but not very character-

* I say that the case given by Hutchinson is the same as Laurence's, after careful comparison of all the available data and in spite of one or two minor discrepancies which leave the identity not absolutely proven. Mr. Hutchinson tells me that the exact date of the original drawing, which would be conclusive, cannot be found (1908).

istic either in form or distribution; retinal vessels stated to have been normal, but when seen again in 1876 they had become shrunken and the discs waxy, although there was no increase of pigment. When seen by Laurence in 1865 she was 7; there were already scattered irregular black deposits in the retina of various shapes, but mostly angular, branched, or linear, and all the choroidal vessels were very plainly visible, the interspaces being paler than the vessels. Laurence described her irides as grey and hair light auburn, her sight as very defective and much worse at night, and her intelligence as dull. When last seen by Mr. Hutchinson (1876), she was about 18, had not begun to menstruate, was very nervous, and was considered by her mother to be losing power in the legs; she was the youngest of 10.—II, 1, ♂, 34 (at date of Hutchinson's account), a fine man, married, and two normal children: II, 2, ♂, 32, a fine man, has five children all healthy. II, 3, ♂, 30, began to lose power in legs when about 4 and became paraplegic, is mischievous and passionate, and has to be under care: at 20 Laurence had found him only 5 feet 3¼ inches high, obtuse in intellect since childhood, sight very defective, especially after dusk, muscular power of legs very defective; fundi showed diffuse incomplete atrophy of choroid, absence of pigment epithelium, and a few scattered pigment spots; in fact, Laurence's description of this young man's fundus might almost be applied to Hutchinson's illustration of the sister's eye. II, 4, ♂, pitted by small-pox, 4 feet 6½ inches high when 18, legs semi-paralysed; sight began to fail at about æt. 6, especially at night; fundi show changes like those in the other cases, but the choroidal atrophy much more advanced, "the fundus has the appearance of a diffused staphyloma posticum"; Hutchinson found much the same 10 years later. II, 5, ♂, died of small-pox, æt. six weeks. II, 6, ♂, 4 feet 4½ inches, dull and inanimate like the other affected brothers; legs not so weak as the others, and could run about well till æt. 6; V. failing since æt. 12, worse at night; fundi as in 3. Refraction H. in all those affected; Fs. stated to be apparently of full size, but there was nystagmus and eccentric fixation.

In all the affected males, development of the sexual organs was arrested, being, according to Laurence, no larger and less perfect

than those of a child of 12 months, but the mammary glands were developed; in (II, 10) no menstruation had occurred at 18. Laurence suggests that the general condition may have been allied to cretinism. The family history, fully enquired into by both authors, affords but little help; the parents were not consanguineous in any degree; there was no evidence or history of syphilis; the father, a tall, well-built, intelligent man, with perfect sight and normal fundi (Laurence), died in a sort of fit, lasting a few hours at the age of 52, having for some time before had a good deal of headache, and on one occasion numbness of left foot (Hutchinson); the mother, still living and healthy in 1876, was an only child, and knew of no nervous diseases in her relatives (Hutchinson): Laurence had fully examined her eyes 10 years earlier and found them normal; she was about 20 when she married. The father was one of six, 3 ♂ besides himself and 2 ♀, the ♂ had no issue, the ♀ both had children who are all normal (Hutchinson).

Congenital Absence of the Choroid.

A few cases have been described where little or no ophthalmoscopic appearance of the choroid existed except over a small area at the y.s. No anatomical examination has yet been made. It is, perhaps, improbable that the condition is related to retinitis pigmentosa; but for clinical reasons the cases may well find a place next to those last considered.

The deficiency of choroid in these remarkable cases is probably congenital, and if so it may date from an early period of development, for the ophthalmoscopic appearances show not merely absence of pigment from the choroidal stroma, but almost entire want of blood-vessels except sometimes certain of the venæ vorticosæ. The clinical features also point to the condition being developmental rather than pathological, or if pathological to the cessation of the morbid process long before birth. For the patients have all told the same tale, that their sight has never been different and is not getting worse, and in Cases 133 and 134 we know that during a period of 5 and 6 years respectively no change took

place. It is difficult to conceive of intrauterine disease causing such profound atrophy of choroid and yet always stopping short at exactly the same part (y.s. area), and thus always leaving fairly good central vision. Moreover, in Case 133 there were indications of choroidal structure towards the periphery, not in patches, but rather as a general, incomplete, vascular development. The integrity, or comparative integrity, of the retinal vessels, again, in nearly all of the cases is difficult to reconcile with a progressive process like retinitis pigmentosa; for in the latter we know of very few cases in which the retinal vessels do not eventually shrink and V. fail correspondingly. The almost invariable presence of some scattered spots or patches of pigment seems at first sight inconsistent with a merely developmental arrest; but the pigment of the retinal epithelium is laid down in man in the first few weeks of embryonic life, before the choroid which is to nourish it has been differentiated; therefore if afterwards the choroid atrophies or does not develop, we should expect that the epithelial pigment, so far as it had been formed, would retrogress and migrate. The escape or relative escape of the blood-vascular system of the retina, and probably, therefore, of the inner layers of the retina itself, and the apparently almost normal condition of the optic disc, though puzzling, seem to consist as well with a developmental as a pathological theory of origin.

Case 130.—Mauthner* (1872). Male, 32; irides bluish green, pupils black and movable; night-blind since childhood, but sight worse since typhoid 15 years ago; now R. My. 3 D., V. 5/200; L. My. 2 D., V. 10/40; Fs. much contracted (in R. about 20° at best = upper part; L. less contracted, kidney-shaped, entirely absent below); O.Ds. hazy, retinal vessels normal in origin and distribution, arteries somewhat narrowed, but otherwise normal; fundus generally of glistening greenish-white colour, owing to the absence of choroidal tissue, except at y.s., where in each eye a network of choroidal vessels is present;

* I have not been able to see the original. The above account is from the detailed abstract in Nagel's Jahresbericht, vol. iii, p. 211 (for 1872), supplemented by Cutler's account in Knapp's Archives, vol. xxiv, p. 337.

in the L. this y.s. patch is sharply defined, rhomboidal, and reddish brown. Some small masses of pigment in places, and a few normal-looking choroidal vessels as in coloboma. A brother believed to be similarly affected. Mauthner described the case as choroideremia, but Leber (G. and S., V., 642) thinks it may have been pigmentary atrophy of retina, with extreme atrophy of choroid.

CASE 131.—Koenig* (1874), from the practice of Professor Schirmer, Greifswald. ♂, 20, asked exemption from military service because he could not see in the dusk and by lamplight; could see well by daylight; his sight had been thus from his earliest recollection. Parents and grandparents saw quite well; consanguinity not mentioned. Patient the first born of nine; a younger brother, age not given, affected in same way; the other seven see quite well. Patient reads small print accurately, but with difficulty, even in somewhat lowered light; colour V. good; Fs. somewhat contracted by daylight (40°—70°), but in moderately darkened room extremely contracted (from 4°—11° in the various meridians). O.D. natural colour, retinal vessels quite normal in all parts; over nearly the whole fundus in each eye reflex is quite white from absence of choroidal tissue, but the y.s. region, where chorio-capillaris is still present, has more or less normal red colour; and a few large choroidal vessels are seen in various parts, especially above O.D. in R. eye. A few pigment patches at periphery lying behind the retinal vessels. Appearances in younger affected brother almost exactly the same, but the pigment deposits rather more numerous, more angular, and elongated; retinal vessels quite normal; Fs. show same character as in elder brother. Author says in the whiteness of the affected parts of the fundus these cases strongly resembled coloboma of choroid, only not limited to lower part, and the boundaries between complete and partial absence of choroid not abrupt.

CASE 132.—Cowgill;† ♂, 17; sight had always been very poor. R. My. 13 D., V. with −8 D. 10/200; L. My. 16 D.,

* Koenig, Zwei Beobachtungen von mangelhafter Entwickelung der Chorioides verbunden mit Hemeralopie, Inaug. Dissert., p. 17 (1874).

† Cowgill, Archives of Ophthalmology, vol. xxi, p. 105 (1892), with semi-diagrammatic illustrations.

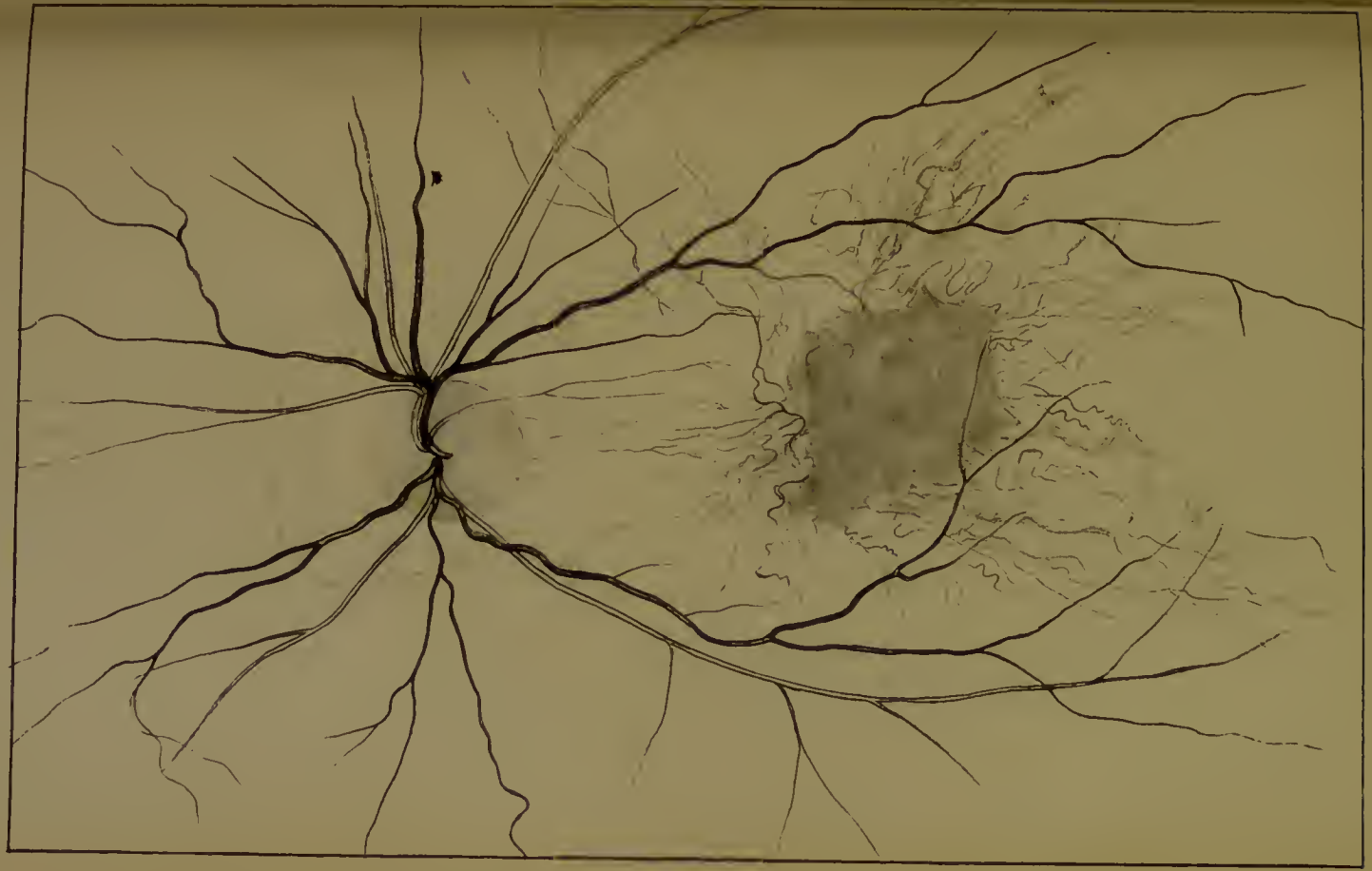
V. with −8 D. 8/200. Whole fundus of scleral whiteness; no choroidal pigment or vessels except a rich plexus forming a nearly circular patch about the size of O.D. at the y.s., and fed by large trunks (one in R. eye, two in L.) that emerge from sclerotic close to temporal side of O.D.; they are flat-looking, without cylinder reflex; central retinal vessels normal in size, number, and distribution.

Case 133.—Bullar (1898).* A case of "deficiency of the choroid." ♂, aged 16 when first seen in 1892; My. 5·5 D., V. corrected R. 6/18, L. 6/12; had always had bad sight, but no note as to night-blindness; Fs. consisted of a small central area of less than 10°, and of a peripheral part about 10° wide lying between the 50° and 60° circles; in R. this seeing part formed a complete zone; in L. it was a crescent occupying the down-out quadrant and the nearest portions of the two adjacent quadrants, *i.e.*, in all about 100 of the circle. Greater part of fundus greyish-white with scattered pigment spots, red reflex being limited to a small patch at y.s. region and around O.D.; some isolated choroidal vessels at periphery, where there is a faint red tinge. In October, 1897, the My. had increased to 7 D. in each, but V. corrected was as good as before. He has five brothers and two sisters; two brothers besides himself have bad sight, but have not been seen; the other four siblings see well.

Case 134 (with Plate XI).—Tatham Thompson (1899)† has described a case of "Congenital Deficiency of Choroid," and has kindly sent me some further particulars and the pencil sketch of the fundus made by himself in 1898 from which the Plate is taken. ♂, 18 in 1898, from early infancy had held objects very close to his eyes, and been able to see only straight in front or by "peering round" at anything; My. 3 D., V. corrected 6/9 each eye: Fs. reduced to less than 10°; marked night-blindness; pupil reflexes normal; fundus everywhere dazzling white from absence of choroid, except at y.s. region, where chorio-capillaris and large vessels are present and give a red colour; a single spot of pigment in L. eye is shown in the illustration; retinal vessels normal or

* Bullar, O. T., vol. xviii, p. 183 (1898); with some additional particulars furnished by Mr. Bullar lately.—E. N.

† Tatham Thompson, O. T., vol. xix, p. 140 (1899).



Leonardson & Co. lith.

perhaps slightly undersized; O.D. showed as pale pink in contrast with surrounding white. Seen again in 1904 and condition unchanged. No consanguinity of parents. No syphilis or tubercle. A great-uncle suffered badly from night-blindness. Patient is one of 11 siblings, of whom three died in early infancy and eight are living.

Case 135.—Landemann's* (1906); ♂, aged 44. Sight bad all his life; sees very badly in going from one illumination to another; in walking keeps head down and narrows the palpebral fissure like an albino; ps. small, act slowly to light, irides dark blue; colour V. good; F. reduced to about 3°; V., R. −1 D. 6/8; L. 6/18 not improved; general fundus reflex shining white; O.D. white; its central retinal arteries and veins much narrowed; a plexus of choroidal vessels at y.s. region, forming a patch as large as O.D., and some vessels passing from there upwards; a few small spots of pigment scattered over fundus; no other choroidal vessels, except some large, probably vortex, veins, three in R. eye, two in L., into which vessels from the macular plexus pass; no cilio-retinal blood-vessels and no trace of long posterior ciliary arteries. Author thinks arrest in choroid and retina causing total obliteration of long posterior and almost total of short posterior ciliary arteries, except those that supply y.s.

Case 136.—Rosenbaum,† in his thesis (1900), mentions in the briefest outline a case (his No. 25) that may have been of this kind; double retinitis pigmentosa with "albinotic fundus" in a patient of 30 with V. 8/18.

Retinitis Punctata Albescens.

Several conditions have received this title. The name should be restricted to the cases, apparently quite rare, in which the fundus is sown pretty evenly with innumerable, discrete, white dots, entirely free from pigment, dull or dead like white paint, affecting the central region as well as or even more than the periphery, apparently dating from birth

* Landemann, A. f. A., vol. liv, 1, S. 63 (1906), with two illustrations (semi-diagrammatic).

† Rosenbaum (Otto), Über Retinitis pigmentosa, Kiel (1900).

or early life and remaining, so far as is at present known, stationary; the dots are always small, and may be invisible by the indirect method. The disease is a family one, but has not, I believe, hitherto been seen in more than one generation (siblings). The parents are often consanguineous. Acuteness of V. may be much, or scarcely at all, damaged, but there is usually night-blindness dating from earliest recollection; in some cases the defect appears to be due, at least in part, to extremely slow adaptation, rather than permanent lowering of light perception. In some, where the zone of dots was incomplete, the unaffected part of the belt corresponded to the situation of ordinary coloboma. The disease does not appear to be related with any one class of refraction. No one who has seen a case will confuse the appearances with those found in any other condition of fundus. But it is difficult to convey in words the difference of aspect between these peculiar cases and those of the various other, more frequent, forms of punctate and dotted fundus change, such as Tay's choroiditis, dotted "honey-comb" choroiditis, the earliest peripheral dotted changes of incipient retinitis pigmentosa, all of which may be due to "colloid" bodies, and even the glancing appearance of Gunn's "Crick dots." Again, study of the recorded cases shows that typical retinitis punctata albescens may occur in the same family with retinitis pigmentosa, and that the characteristic albescens dots may occupy the central region, whilst "colloid" dots are seen at the periphery.

We have, therefore, in retinitis punctata albescens a variety of retinitis pigmentosa, but one that differs widely from the type, not only in the visible changes but in the vitally important practical feature that it is stationary, or, at the worst, almost infinitely slow in progress. Since no anatomical examination has been made, the nature of the white dots is not known, but they look so unlike the spots or dots that are generally considered to be "colloid" growths that I do not think they are of that nature, although, like "colloids," they lie in the plane of the pigment epithelium and elastic lamina,

and sometimes pass insensibly into "colloids" towards the periphery. Is it possible that in these peculiar stationary white dots we have the result of a disease of the chorio-capillaris lasting for a part only of fœtal life, perhaps an early part, ceasing far short of destruction or atrophy, and permitting the resumption of normal growth and development at a later stage? The comparatively uniform dissemination of the spots brings to mind the arrangement of the ultimate arterioles of the choroid in animals furnished with a tapetum; these minute vessels penetrate the tapetum vertically from without inwards, each one dividing on the inner surface into capillaries, which radiate horizontally from the top of the stem like the ribs of a Chinese umbrella. If each one of the white dots of retinitis albescens represented a formation situated at the inner end or top of such an arteriole stem, the distribution of the dots would be explained, for, though the human choroid contains no tapetal layer, the mode of branching of the choroidal vessels is essentially the same as in choroids where that stratum is present.

The term retinitis punctata albescens was introduced by Mooren (5, p. 216, 1882).*

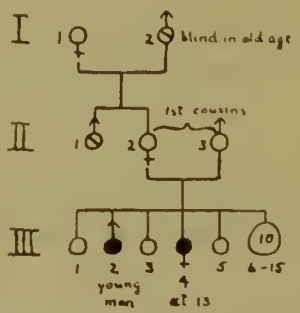
His patient, Case 137, was ♂, aged 30 (1868), whose fundus presented innumerable small dull white dots, sprinkled with tolerable uniformity between the somewhat shrunken retinal vessels; O.D. rather blurred and greyish; retina rather dull in

* In this paper, Mooren says that Kuhnt (then of Jena) had recently shown him an ophthalmoscopic drawing of a similar condition. Kuhnt's case, narrated at "der 55. Versammlung deutsch. Naturforsch. u. Aerzte zu Eisenach, 17—21 September, 1882," was published in Zehender's Klin. Monätsbl. f. A., vol. xxi, p. 425 (1883), and was also personally reported, in brief, by Mr. Story (O. R., vol. i, p. 411, December, 1882). From the above we learn that the patient was a young girl with contracted Fs. and V. reduced to one-sixth, and that Kuhnt had, since seeing her, met with similar appearances in two other cases. Kuhnt described numerous minute white dots in the *inner* layers of the retina with considerable lowering of vision, concentric contraction of F., and inflammatory appearances, all disappearing with return of V. and F. after a few weeks' treatment. The disease cannot have been the same as that we are now considering. Professor Kuhnt (now of Bonn) is unable to supplement the above account (1908).

tone. V. lowered to 1/10 to 1/5; Fs. full both by daylight and lamplight. No alteration occurred during several years. Night-blindness not mentioned. The white dots were never in front of retinal vessels.

CASE and Fig. 138.—Gayet (1883);* a young man and his sister aged 13: ophthalmoscopic illustrations. Brother (III, 2) night-blind from childhood, contracted Fs.; some amblyopia, apparently not getting worse; refraction My. As. 2 D.; retinal vessels rather diminished. Scattered over entire fundus of both eyes—except macular region—from near O.D. to extreme periphery, multitude of white dots, comparable in appearance to the white dots of albuminuric retinitis, but quite differently arranged and not grouped; retina rather grey, but no pigmentation; the retinal vessels lay in front of the dots. Perception of colours defective, so that he had not been able to follow his father's trade of weaver in colours. Hearing good, but absolute want of

Fig. 138



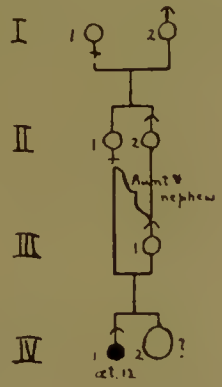
musical ear. Intelligence fair. Sister (III, 4), aged 13, in addition to the white dots showed changes resembling true retinitis pigmentosa at some parts of the periphery; she was also quite unable to distinguish musical tones, and had such poor colour perception that she was unable to learn weaving. No family defects or degeneracies. Parents first cousins, alive and well. Mother's brother (II, 1) had bad sight, and mother's father (I, 2) was blind for some months before he died at 70. The patients were 2nd and 4th members of a childship of 15, but only 5 are specified.

* Gayet, Arch. d'Ophth., vol. iii, p. 386 (1883).

Dor's case (*ibid.*, p. 481), sometimes quoted in this connection, is not characteristic; it has been mentioned as Case 115 above.

Case and Fig. 139.—Fuchs* (1896), typical case. A healthy ♂ of 12 years (IV, 1), only child of union between nephew and aunt; night-blind since 6; central vision full, but F. much contracted; O.D. and retinal vessels normal; fundus—except at periphery and over an area of two O.D. diameters at y.s. region

Fig 139



—sown with pure white, sharply-defined dots, with no marginal pigmentation, and none broader than a retinal artery of the second magnitude; periphery and y.s. region free.

Cases are also mentioned, but not described, by Ole Bull and Krienes.

Case 140.—Byers (1900), typical, but with addition of a patch of old pigmented choroido-retinal disease in coloboma position in R. eye, also a fibrous string *in vitreous*. The patient, ♀, 37 (1900), found to be night-blind when 3; married at 20 and had 3 children, all with good sight (two of them fully examined); no other conceptions. No consanguinity of parents and no other cases known; no note of the number of the patient's siblings. Now V. 6/9, Em., Fs. full in daylight, contracted to about 30° in dull light. At each fundus numerous small, rounded, or slightly oval dots, sharply defined, greyish-white, and with a dull surface; O.D. and retinal vessels normal.

* Fuchs, A. f. A., vol. xxxii, 2, p. 111 (1896).

Case and Fig. 141.—Spengler (1901), atypical, and the accompanying illustration poor. The dots, on the whole, resemble those of retinitis punctata albescens, but in two of the four affected siblings there are also a number of much larger pale yellowish spots in the choroid; in the third the choroid was almost albinotic, both at the periphery and in the ordinary position of coloboma, and in the 4th (II, 4) the whole fundus was so, except the y.s. area. The four patients (II, 1 to 4) were aged between 16 and 12, and, together with one miscarriage (II, 5), formed the whole childship. Only slight amblyopia, no contraction of F., and no night-blindness. Parents 2nd cousins: they, their parents, and grandparents said to have been normal. Compare with Cases 125 to 128, and 130 to 136.

Fig. 141

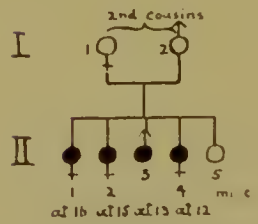
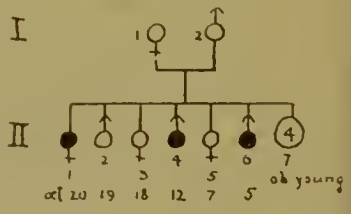


Fig. 142



Case and Fig. 142.—Van Duyse (A. d'Opht., 1907, p. 497) gives three new cases (siblings), with two excellent ophthalmoscopic plates. II, 1, ♀, æt. 20; refraction nearly Em.; black hair, brown irides; Fs. concentrically contracted; night-blindness extreme since æt. 2; colour-blindness, only blue being recognised; Nystagmus, V. only fingers at 3 m.; health good; urine n.; teeth good; retinal arteries rather too small, veins n.; choroid dark, but at periphery some yellowish spots as wide as large retinal veins; innumerable minute dots, white, fairly well defined, sometimes grouped like grapes, behind the retina, most numerous near O.D.; larger, though less numerous, towards periphery. II, 4, æt. 12, black hair, brown eyes; marked night-blindness since æt. 3 to 4; Fs. contracted to 5°—10°; nystagmus; R. My. 7·5 and 6·5; L. 8 and 5·5, normal axes; V. corrected 1/8; in 24 c.p. light cannot count fingers at 30 cm. Fundus shows white dots similar to II, 1, but of much

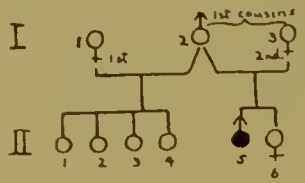
smaller size, retinal arteries shrunken; sclerosis of peripheral choroidal trunks. II, 6, æt. 5, brown hair; more intelligent than the older ones; extreme night-blindness since he could first walk; F. much contracted, as proved by his soon losing light from mirror unless he fixes it; nystagmus; moderate H.As.; white dots at fundi as in the others, but most abundant at periphery; sclerosis of some choroidal trunks. Father (I, 2), 44, normal vision; choroidal vessels not visible. Mother (I, 1), 42, old central nebula L. cornea; V. normal, fundus normal. Had "typhus," æt. 16, no other diseases. Has had 10 children, normal labours, none miscarried or premature. Four died between 10 months and 3 years of pneumonia, "dropsy," or croup; no consanguinity; no syphilis. The normal children :— II, 2, æt. 19, fundus n., Em., V. full; II, 3, 18, R. low My., L. M. As., 3·5 normal axes, fundus n.; II, 5, 7, fundus n.; slight H. As.

I have seen cases in the following four families :—

Case and Fig. 143 (unpublished).—II, 5 ♂, 31 (P. 24, 6) (1891). As long as he could recollect he had seen badly in dull light, used to be teased about it when a boy; it was not getting worse. In good light could see perfectly. It was in truth extremely slow adaptation to dull light rather than permanent dusk-blindness; an exposure of only three or four minutes to sun-light would blind him, so that for the next five minutes he could not find his pipe in a shady room; after two hours in the afternoon sun, in Florida (where he had lived for the last year), was so blind at sunset that for from half an hour to an hour he could not see a man sitting close to him, as, *e.g.*, in a rowing boat. This night-blindness never lasted longer than an hour, and he believed that after such an interval of rest his sight in the evening was as good as that of other people. V. each 6/6, Sn. Hm. 0·5 D.; Bjerrum's types 6/12 slowly (against my own 6/9). Characteristic white dots of retinitis punctata albescens at posterior part of fundus and as far forwards as equator, but none at extreme periphery; they closely surrounded the disc, where also the nerve-fibre layer of the retina was rather hazy; y.s. itself free from white dots, but the retina there showed a fine mottling; the dots often lay parallel to choroidal vessels

(Fig. 143A); no dots at lower part of equator, and it may be noted that he had once found he could see a little in the upper part of the field when he could not see at all in front; F. (perimeter)—5 mm. test object—quite full in daylight; but with artificial light reduced to the lowest compatible with a full F. in myself, the patient's F. was diminished all round by about 15°. His father had married twice; by first wife, who was not consanguineous, he had four children, all living, and with perfect

Fig 143



sight (II, 1—4). His second wife was a first cousin, and the patient was the first of this union, the father being 47 when he was born; the second and last child (II, 6), two years younger than patient, I examined, and found to have perfect eyes. Patient had abscesses in neck as a child, and was sent abroad for several winters; he died in Florida of tubercular meningitis not long after I saw him.

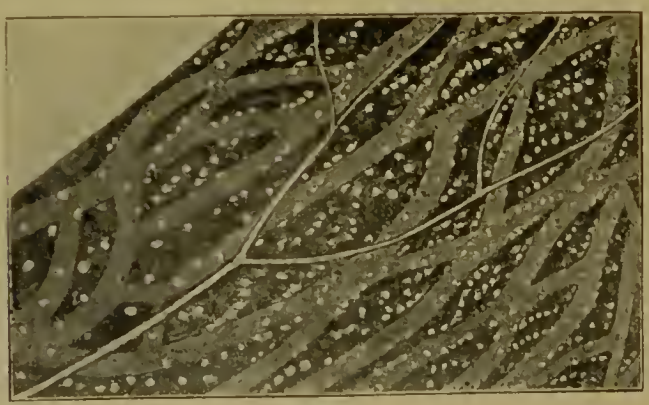
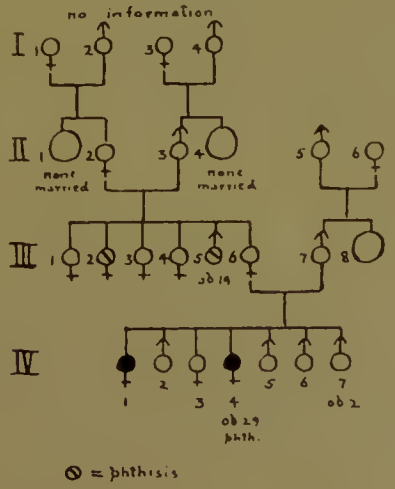


Fig. 143A.—Half diagrammatic study of the white spots of Retinitis punctata albescens in Case 143, II, 5. From a sketch by Mr. Donald Gunn.

CASE and Fig. 144.—Two sisters (published O. T., vii, 301, 1887); I (IV, 1), ♀, 19 (1886). Seen again in 1901 and 1907. Night-blind all her life. H. 3·5 D., V. and F. in good light normal; F. by artificial light 15 mm. test about 10° smaller than n. Cannot go about in twilight or by artificial light unless very bright; can do pretty well by moonlight. Förster's photometer; 10 minutes' adaptation; marked lowering of light sense; sees no light until opening = 27 mm. diameter, whilst her normal brother sees when opening = 2 mm. She was thin and delicate-looking from overwork (teaching), but neither she

Fig. 144



nor her mother had reason to think her ill. At fundus of each eye an immense number of minute discrete dead-white dots at equator, and from there, nearly as far back as O.D.; mostly round, but a few staff-shaped or club-shaped; not arranged in any uniform direction, but scattered at even distances; O.Ds. and retinal vessels normal. Last seen in Autumn, 1907, 20 years after first examination, when she said she was no worse, except that she had lately had stronger glasses ordered by Mr. Holmes Spicer. Fs. to hand, by lamplight, full. The white dots exactly as always, most abundant at and behind equator, not so numerous near O.D., and none at y.s. No spots

at periphery, but the epithelium there has a granular or disturbed or smudgy appearance; this was the same when seen in 1901, and may have been so at the first inspection in 1886. The white dots more abundant in R. than L. Arteries, especially in R., decidedly though slightly smaller than in L.

II (IV, 4), ♀, 14 (1887), and seen again in 1892, appearances the same both times. White dots, exactly like those in IV, 1, but more numerous; "they look as clean as if newly made yesterday;" they are wanting in the down-in part of each equator. In front of equator, where they cease, the stippling of the pigment epithelium is coarsened, and ill-defined pale spots, apparently thinned choroid, are seen, and further forward, at extreme periphery, some defined circular dots of same size as the typical white dots, but less white, and surrounded by pigmented collars like "colloid" nodules. H. 4 D., V. corrected 6/9 partly; no glass gives 6/6. Dusk-blind like IV, 1. Died of phthisis in 1902 aged 29, sight having remained the same.

IV, 5 seen more than once; is H., but his eyes healthy and sight perfect. IV, 2, 3, and 6 all healthy, with perfect sight. Whole childship (IV, 1—7) born at full term; no miscarriages or still-births. Parents not consanguineous. Mother (III, 6) had good health until her death from cardiac failure after pneumonia early in 1907; she was the last born of six, and much younger than the fifth (III, 5), who died of phthisis at 14; III, 2 also died of phthisis. Father (III, 7) died of diabetes at 48, was one of a small childship, and had no nephews or nieces.

CASE 145.—Two sisters (*ibid.*, p. 303) I, ♀ (Mary), 18, R. H. 3·5 D., V. 6/6; L. − 3·5 s. + 1·5 c. 6/12; periodic convergent squint of the R. (better) eye. Fundus changes mostly of the kind described, as at the periphery in Case 144, IV, 1; but here they occur all round the equator, and back nearly to O.D.; choroid mottled with small whitish spots, some semi-confluent, some sharply defined, but the majority not so; at periphery much deposit of pigment, but not reticulated as in retinitis pigmentosa. O.Ds., retinal vessels, and y.s. normal. Difficulty in seeing by twilight as long as she can remember, but not getting worse; rather deaf, stupid, and bad tempered. No

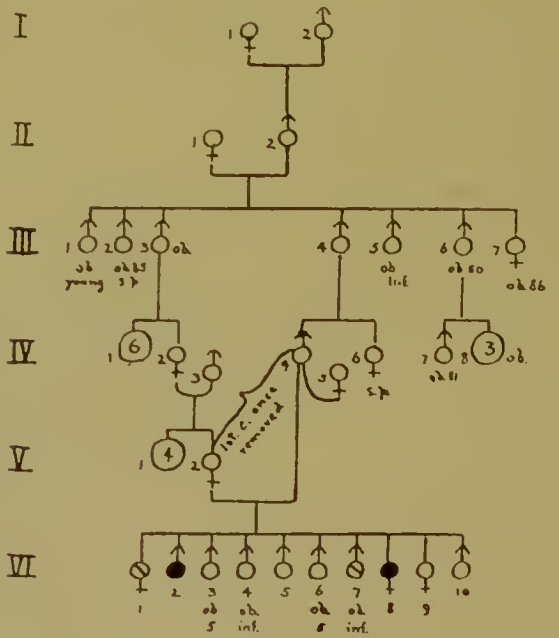
signs of hereditary syphilis. Much of the change is such as would be explained by the growth of "colloid" or "drusen" bodies on the elastic lamina of the choroid.

II, ♀ (Lizzie), 17; typical dead-white dots thickly sprinkled from equator back as far as macular region, for most part smaller than diameter of principal retinal vessels; all lie deeper than retinal vessels in front of equator changes, resembling those in sister (I), but with less pigmentation; O.D., y.s., and retinal vessels n.; slight H., V. full, but sees badly by twilight or artificial light. Rather deaf. Seen again, æt. 22; thought her night-blindness worse; but was nervous and out of health, and I was not convinced that her eyes had really deteriorated; V. still 6/6; the appearances had not altered; multitudes of small, very white, separate dots, generally equidistant, but sometimes arranged in rows; y.s. not affected; O.Ds. and retinal vessels n. Two or three O.Ds. from O.D., the white dots gradually gave place to more general disturbance of pigment epithelium, and at periphery are irregular collections of pigment with exposure of intervening choroidal vessels. As the white dots pass into the pigmented zone, some of them show a minute central black point, and such centrally pigmented spots are partly confluent. This final note is important, as showing clearly a gradual transition of the white dots into changes probably of the "drusen" type. These sisters showed no signs of inherited syphilis; they were the two youngest and only survivors of eight; the six elder died in infancy; no details obtainable. Father alive (1886) and well; mother died æt. 46, one year after the birth of Lizzie, from lung disease of some kind. Consanguinity not mentioned.

Case and Fig. 146.—VI, 2, published, O.T., viii, 163 (1888), with coloured plate; additional details, 1905. November, 1887; ♂ (VI, 2) aged 21, healthy, strong, intelligent lad, working on his father's farm. No signs of inherited syphilis; did not have scarlet fever when his sibs. had it; as long as he could remember had been unable to see well in the dusk. V. with slight H. As. corrected R. 6/9 (not 6/6), L. 6/12. At posterior polar area numerous single, minute, very white dots, evenly distributed, not grouped, free from pigment; they come close up to fovea centralis closer in L. than R.; subjacent choroid looks perfect;

anteriorly the spots gradually thin off, but there the epithelium becomes disturbed and choroidal trunks visible; further towards periphery choroid even paler, and shows a little granular pigmentation; O.Ds. slightly hazy; retinal vessels n.; nothing like retinitis pigmentosa anywhere. Fs. in daylight reduced concentrically by 10°—15°; in dim light reduced to the 20° circle. Seen again in 1894, and no change found. Seen finally in December, 1905, aged 39, 18 years after first examination;

Fig 146

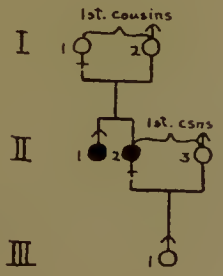


probably no change has occurred; V. of each eye is exactly as at first, and the only additional note is that the white dots are rather larger in L. than R.; O.Ds., vessels and periphery as before; does not consider himself any worse except that he thinks his sight does not adapt so quickly to changes of light as formerly; "if I have been for half an hour in brilliant sunshine and then come into a room I am in pitch darkness for about five minutes; I have always had this difficulty, but I think it has got worse lately." At both examinations (1887 and 1905)

it is noted that at some parts of equator there are no changes at all, neither white dots nor choroidal disturbance. He (VI, 2) is second born of 10, and the fifth male bearing the same christian and surname in direct descent. One younger sister (VI, 8) has the same disease; when a child at school could not find her way home alone on dark winter afternoons; gets no worse. I saw her December, 1905, aged 32; V. each 15/30; slight H.; Fs. in daylight full (rough test with fingers); same test applied when the blind had been let down showed decided contraction; the appearances resembled those in her brother (VI, 2), but the white dots smaller and much more numerous, "thousands" one would say; epithelium at periphery altered, as in the other cases—removed in some spots, accumulated in others—but no coarse collections of pigment, and nothing in the least like retinitis pigmentosa. Parents (V, 2, and IV, 4), first cousins once removed; mother (V, 2) married at 26 and died of influenza at 53; till then had good health; all her children except VI, 2, born at full term, but none were suckled; VI, 2, born at 7 months, was very small, and only 9½ months younger than VI, 1. Each of the two night-blind children was immediately preceded by a child with hare-lip (VI, 1 and 7); of these two I examined VI, 1, in December, 1905, æt. 40, and found the eyes quite normal except slight My. Of the 10 children (VI, 1 to 10) 4 have died; VI, 3 and 6 at 5 years, 4 in infancy, 7 (hare-lip) in infancy; 6 are living and aged between 40 and 22. In other respects the pedigree explains itself.

Case and Fig. 147.—Griffith (O.T., xvii, 51, 1897). ♂, 48 (II, 1), night-blind all his life, and was apparently not getting

Fig. 147



worse; refraction almost Em.; V. only 6/36; Fs. full for white in daylight; no central or ring scotoma; colour-vision good; O.D. pale and waxy, retinal vessels slightly constricted; the whole fundus shows a mottled appearance, "but especially round the disc and macular region there is a ring area covered with discrete yellow spots resembling Tay's choroiditis." Parents first cousins. Patient's sister (II, 2) suffers from night-blindness; she also has married her first cousin, and has a son whose sight is perfect. The description of the spots is not quite characteristic, but in all other respects the case is typical.

The following cases, though not all typical, are important; *two of them*, 149 and 76, show *ordinary retinitis pigmentosa*, and what seems to be *punctata albescens side by side in the same family.*

Case 148.—Groenouw (1902). Author's family 2. 1. ♀, æt. 9, first born of five. Night-blind with much contracted Fs. My. 1 to 2 D., V. 2/3 corrected; entire fundus sown with small white spots, roundish and situated behind retinal vessels; O.Ds. n. II, æt. 7, ♂, examined and found quite normal. III, ♀, aged 5, third born; bad sight, especially in the dark; too restless for good examination; choroid very blond, but not that of a true albino, perhaps a few small white patches; no pigment spots. No note as to fourth and fifth. Father, 37, "always" night-blind, but until 32 could see well in bright light; since then sight gradually failing, and now only fingers at 1 m.; has all the changes of advanced typical retinitis pigmentosa; knows nothing of his own parents. Later observations on the children would be valuable.

Case 149.—Wnestefeld (1901) (with coloured plate). ♀, 8, night-blind for long, now with My. 5 D. and 7 D. in R. and L., corrected V. 2/5 in each, C. V.n.; Fs. much contracted in dull light, but full in daylight; light sense (Förster's photometer) = 1/30. Choroid extremely dark; O.D. rather pale; retinal arteries about normal; fundus showed a multitude of small white dots reaching close to O.D. and Y.S., free from pigment, the smallest only just visible in inverted image, the largest three times the diameter of retinal vessels of second magnitude: the

dots follow no uniform direction, though some lie alongside vessels; none are in front of retinal vessels; they are so numerous as to give a whitish aspect to the retina, some choroidal vessels bordered by white. A younger brother, aged 6, also night-blind, but not so badly. V. of each 2/3, H. = 0·75 D.; too young for Fs. and light sense. Choroid very dark; no white dots as in the sister, but at the periphery retinal pigmentation in fringed almost bone-corpuscle-like deposits; O.Ds. and retinal vessels normal. No consanguinity. No syphilis. No note of other siblings.

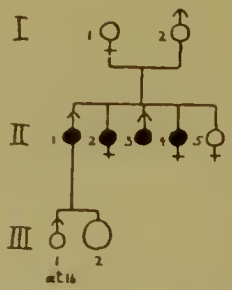
Case 76.—*Retinitis punctata albescens (?) and retinitis pigmentosa in different members of same childship, all adult* (see pp. 37—38, with Fig. 76). The childship III, 1 to 11, originally consisted of 12, order of birth not noted; 10 are grown up, and 9 living, 7 ♂, 2 ♀. Three ♂ and one ♀ are night-blind, and three of these have been examined at one time or another by four ophthalmic colleagues. Two ♂ (III, 11) died young, one of "water on the brain"; the third who died was III, 4, mentioned below. Parents first cousins. No earlier history of night-blindness known, but enquiry incomplete. The three cases were:—

III, 1, ♀, 38 in 1896; had noticed night-blindness four or five years; Fs. nearly Em., V. R. 6/18 part, L. 6/12 part; "media clear, numerous fine, dull white dots chiefly at periphery; O.Ds. healthy, retinal vessels of fair size, Fs. contracted": seen by a different surgeon in 1905, aged 47 or 48; V. not in the least worsened, "O.Ds. rather pale and retinal arteries too small, no pigment deposits." III, 2, ♂, 43 in 1905, noticed night-blindness for the last year or two; V. with slight H. As. corrected R. 6/5, L. 6/6; "definite retinitis pigmentosa of typical character at periphery of both eyes; O.Ds. rather pale and retinal arteries too small, especially in L." One of his children, ♀, æt. 11 (not shown in Fig. 76), examined and eyes found healthy. III, 3, ♂, reported to be night-blind, but not seen. III, 4, ♂, examined when a student at College in 1895, aged about 20, was night-blind and intellectually dull; "no retinitis pigmentosa, but at the periphery numerous discrete white spots"; he died of pulmonary tuberculosis as a young man. In this family the white dots were confined to the periphery, and night-blindness was not noticed until about 20 to 30 years of age. One of them

had typical retinitis pigmentosa and no white dots, and he asserted that his night-blindness was not noticeable till he was about 40.

Case and Fig. 150.—Liebrecht* (1895) saw two brothers and a sister, and heard of a second sister similarly affected, in a childship of five; only the youngest escaped. II, 1, seen by Alfred Graefe, 1872, æt. 26; V. 22 Jäger at 3 m. and 3 J. read with difficulty; Fs. full, but a small defect at centre; central circumscribed chorio-retinitis with dirty white spots and some pigment changes, no night-blindness; 1881, V. 1 6 and 3 J., Fs. full, central defect as before, no proof of any new changes; seen by Liebrecht, 1895, æt. 48, V. fingers at 4—5 m., with +8 D., some words of 1·6 Sn., colour V. normal; F. full to rough test, no scotoma; O.D. somewhat pale, vessels normal;

Fig 150



fundus everywhere showed small dull white spots most abundant near O.D. and y.s. getting fewer towards front, almost absent at periphery; not disposed in any definite relation to retinal vessels; free from pigment, not very sharply defined, and measuring from 1 to 4 times the diameter of the retinal vessels; vessels often pass over the front of these spots; no signs of inflammation or hæmorrhage; general condition good; no albuminuria; V. of late much worse on going into the dark. Has children, of whom the eldest (III, 1), aged 16, complains of his sight, but has not been examined. II, 2, seen by Graefe (1872), Fs. full, V. 8 J. well, was similarly affected; changes as

* Liebrecht, Klin. Monatsbl. f. Augenheilk., p. 169 (1895).

in II, 1; seen again by Graefe in 1881, but not by Liebrecht in 1895. II, 3, seen by Graefe, 1872, æt. 24, Fs. full; fine, pale, roundish changes, not pigmented, at posterior polar region only; some My. As.; V. with correcting cylinders 3 J. fairly; in 1895 Liebrecht found same conditions as in II, 1. II, 4, seen for the first time by Liebrecht, 1895, æt. 41; V. had been failing 15 to 20 years; could still read large print with +5 D., *i.e.*, better than her elder siblings at same date: fundus changes, Fs. and colour vision same as in the others. Parents both good sight and not consanguineous. No syphilis. No heredity.

This narrative is of special interest, from the length of time (23 years) during which the patients were under notice, but judging from the description I think the disease may have been a variety of family choroiditis; the spots were larger than in retinitis punctata albescens and the disease was perhaps progressive. Liebrecht's case may perhaps be compared with Juler's* and Doyne's† cases (Honeycomb Choroiditis, etc.). Lang's case‡ (O.T., v, 140 and 141) (1855) in a brother and sister must also be classed clinically as family choroiditis.

Congenital Night-blindness without Changes.

Night-blindness was known long before the ophthalmoscope had been invented, and observers were aware that the condition might be either temporary and curable, or permanent; that when permanent it might be either stationary or progressive; and that the permanent forms of night-blindness often attacked several members of the same family. Night-blindness was, and still is, sometimes called "moon-blindness," although one of the points generally made by the victims is that they are not blind in bright moonlight. Underlying this name was no doubt the idea that sleeping in moonlight caused the disease. There is probably some truth in this tradition as regards the temporary or

* Juler, O. T., vol. xiii, p. 143 (1893).
† Doyne, *ibid.*, vol. xix, p. 71 (1899).
‡ Lang, *ibid.*, vol. v, p. 141 (1885).

endemic form of night-blindness which occurs under circumstances of combined privation and prolonged exposure to light; at such a time a long night in the dark might retard the onset of the disease, whilst exposure of the uncovered face to brilliant moonlight, as in sleeping on deck or without tents on the march in a tropical climate, might materially assist in precipitating an attack. There is no proof that exposure to light influences any of the forms of permanent night-blindness.

With the ophthalmoscope came the discovery that lasting night-blindness was usually explained by visible choroido-retinal disease, and that after deducting from such cases those of syphilitic choroiditis (the diagnosis of which was difficult in only a few instances) the greater part of the remainder fell into the class we have been considering as retinitis pigmentosa or one of its near kin. But a small residue of cases was left in which, although the night-blindness was a permanency, no ophthalmoscopic changes were present; and enquiry showed that in these not only was the peculiar visual defect always present from the earliest age (a few months or a year) at which any tests could be applied by the mother—and doubtless in reality from birth—but that it did not get worse; it also presently appeared that this form was, like retinitis pigmentosa, often hereditary.

The first systematic account of this congenital stationary night-blindness was, I believe, the short one given by Leber in 1877.* Soelberg Wells, in his admirable treatise published a few years earlier (1870), had not mentioned the subject, and this probably indicates that it had not attracted the notice of Von Graefe. Since Leber's account, the subject has not received much attention from systematic writers. The malady may, perhaps, not be so rare as is supposed; being innate and non-progressive, it may sometimes be overlooked, or taken as a natural peculiarity, or occasionally may be concealed. Our clinical knowledge of the disease, or diseases—

* Leber, Graefe-Saemisch Handbuch, vol. v, p. 649, § 89.

for there are signs that the cases now provisionally classed together are not all alike—leaves much to be desired, whilst as to the nature and seat of the mischief, no more is known than in the case of colour-blindness. In the absence, hitherto, of microscopical examination, nothing can be said as to the finer condition of the retina. Nor can it even be asserted positively that the eye itself is at fault in all cases: when the night-blindness is—as in one sub-group—correlated with myopia, the defect must, one supposes, be peripheral; but in the perfectly uncomplicated form the seat of the defect might be central.

The descriptions of their condition given by the subjects of stationary night-blindness resemble each other closely. They can see pretty well by lamplight or by bright moonlight, but on moonless nights, or if they go into a darkened place, such as a cellar, in the daytime, they are blind; the children in such circumstances walk with head erect and arms extended; as adults they apparently learn to perceive the presence of obstacles by some movement of the air; on a moonless night, unable to see the roadway, they guide themselves by looking up and detecting the sharply-cut lines of the house-roofs against the sky. The subject, IV, 9, in Case 177, a gentleman of scientific tastes and an acute and very trustworthy observer, after reading the recently published account of the Cunier case (Case 151) wrote to me as follows:—"The account is of special interest to me, as I find that I naturally do the same things. I have a hand moving in front when in any doubt as to surroundings, and when out alone at night I invariably look up to catch the outline of trees, etc., against the sky unless the latter to me is absolutely black. In what is to me complete darkness I can, without a stick, get along fairly well by feeling the contour of a road or the junction of the roadway and grass. Naturally I have often come to grief when out alone at night, *e.g.*, I three times walked into the canal near my father's house, twice in consequence of thinking a certain light was from one lamp when it was from another, and the third time because I had gone a little further

than I thought. Again, I have walked over a wall and fallen 6 feet into a sunk road; once when walking fast through a village at twilight I cut my face open against a lamp-post, and as a boy I have run into many wheelbarrows and iron railings, and even a horse and cart standing still. At the same time," says Mr. ——, and this is of great interest, "I have never run into a wall or a tree of any size; I always detect the proximity of such a large solid object, sometimes by heat radiating from it, sometimes by a change in the air currents, but much more often by sound—the echo of my own footsteps. I can see very few of the stars, I think only the first magnitude; and though I can manage to get about in gas-lit streets I do not like doing so unless the ground is wet, and I can then see the reflections of the people and vehicles I meet." He then describes how his defect has been, in special circumstances, actually a boon and safeguard. "In a fog, and especially at night, I have on several occasions acted as guide to people with normal sight, as I was used to looking out for such signs as I have named above, and was also a fair judge of the distance travelled. I remember once, when I was a boy, being out with friends near the sea, in the daytime, when a thick fog came on, and as we hurried along through a grass field I suddenly stopped and called out; we all listened, and heard the sea breaking below us, the edge of a cliff which we thought a quarter of a mile off being a yard in front of us; I think it was an air current I felt, as the sea was very calm."

According to present knowledge—admittedly very imperfect—the cases classed together in the present section as "congenital stationary night-blindness without changes" do not really form a homogeneous class, but must for practical purposes be subdivided into two principal groups. In both groups the night-blindness is strongly marked and accompanied by contraction of the field when the light is much lowered, and no length of stay in the dark enables the affected person to see any better; and in both the condition is hereditary.

In the first group the night-blindness is not correlated with any other condition; visual acuteness is normal in most, probably in all, if allowance be made for various refractive errors in some of the less educated subjects; the fundi are absolutely healthy; refraction normal, or, if abnormal, not always erring in the same direction; both sexes suffer in fairly equal numbers; either parent may transmit to children of either sex; and descent has been continuous in the pedigrees that have been most carefully worked out. In regard to sex and usual mode of descent, in fact, this variety agrees with retinitis pigmentosa.

In the second group the leading features are myopic refraction; limitation of the disease to the males, but transmission through the females; visual acuteness with correction, often, but not always, subnormal; nystagmus sometimes present; slight ophthalmoscopic changes sometimes found, though their inconstancy throws doubt upon their relation to the disease. We do not know how the three characters, night-blindness, myopia, and male sex are related in this group. There is, however, reason to think that in many, if not all, of the cases the myopia is present at birth, and we are therefore tempted to ask whether both the abnormal ocular conditions may not be due to disease in fœtal life which has led to a limited elongation of eyeball and damage of choroid and retina before these structures are fully developed? At this point attention may conveniently be drawn to the complaint of seeing badly at night brought by some ordinary myopes. I have not been able to satisfy myself that this difficulty was due to anything more than the blurred images of uncorrected myopia aided by poor illumination. The field of vision is said by those who have paid special attention to the point to be somewhat smaller in myopic than in hypermetropic eyes, but it seems doubtful whether the contraction is enough to cause symptoms. Moreover, this loss, such as it is, being a result of the elongation of the eye and consequent removal backwards of the anterior limit of the sensory retina ought to, and I believe does, in

general terms vary with the degree of myopia. Therefore if it were the cause of such lowering of function of the retinal periphery as could cause marked night-blindness, we should expect always a high degree of myopia in such cases; and further, we ought to find night-blindness in every case of high myopia, and such is very far from being true; for whilst 11 D. is the highest My. recorded in any of these hereditary night-blind patients, from 3·5 D. to 9 D. are the ordinary figures. I think, therefore, we must conclude that when certain males of a given genealogy are both night-blind and myopic, the conditions are not respectively cause and effect, but are related to some other and common factor.

Returning to Group I: descent, as already mentioned, is continuous in the majority of families, and when continuous in one part of a given genealogy is invariably so in all. In a few pedigrees, nearly all of them very incomplete, the parents of the affected children were reported to be normal, *i.e.*, inheritance was discontinuous; it is probably an accident that in this small series there are only 9 ♂ affected to 14 ♀, whereas in some of the families where descent was continuous the sexes were practically equal, as the following table shows:—

TABLE B.—*Congenital Night-blindness. Group I. Descent continuous. Both Sexes affected.*

	♂	♀	Total.
Cunier's case. Gens. IV, V, VI, VII, VIII (excluding Gens. I, II, III, and IX as probably incomplete)	59	52	111
Others, viz., Cases 152 to 157	17	23	40
	76	75	151

We want for comparison to know the proportions of the sexes in the unaffected and in the total of affected + unaffected in the same families.

This cannot be given for the whole series, because many genealogies are either incomplete or contain items whose sex is not given; but we may probably, without serious error, use for this purpose those in which the sexes of all are stated, and these give the following results:—

TABLE C.—*Sex in the Normal Members of the Childships that furnished Table B* (omitting childships in which the sex of any was unrecorded).

	♂	♀	Total.
Cunier (as in B)	81	52	133
Other cases (as in B)	21	16	37
Total normal in diseased childships	102	68	170
	♂ + ♂	♀ + ♀	Total.
Diseased + normal in diseased childships	178	143	321

TABLE D.—*Sex in the Unaffected Childships of the same Genealogies* (corrected as above).

	♂	♀	Total.
Cunier (Gens. as in B and C)	764	758	1522
Other cases (Cases 153 and 156 only; no others complete)	7	6	13
	771	764	1535

Compared with completed pedigrees of retinitis pigmentosa, we have the following:—

TABLE E.—*Retinitis pigmentosa. Number of each Sex in Affected Childships* (corrected). (Corresponding to Tables B and C together.)

			Total.
Affected members.....	♂ 121	♀ 92	213
Healthy members of diseased childships	♂ 103	♀ 111	214
	♂ + ♂ 224	♀ + ♀ 203	427

TABLE F.—*Unaffected Childships of the same Genealogies as Table E* (corrected). (Corresponding to Table D.)

♂ 72 ♀ 71 Total, 143.

These numbers are almost exactly one-third of those in the disease-bearing branches, and if tripled would be

♂ 216 ♀ 213 Total, 426.

From Tables B and C we conclude, assuming the correctness of the data, that females are rather more liable to congenital stationary night-blindness than males, as has always been the tradition in the Cuvier family, Case 151; the reverse of the rule for retinitis pigmentosa (Table E and pp. 49 and 338).

Relative Liability of the Sexes to Transmit the Disease.—In the Cuvier case, the affected men who married transmitted the disease less often than did the affected women who married (51 night-blind men married and 46 had children, 30 of the 46 had night-blind children, 16 had all normal children, or 2 to 1; 47 night-blind women married, and all had children, 36 of them had affected children, 11 had all normal children, or 3¼ to 1). In the six other best pedigrees* the corresponding numbers are as follows:—Of 19 night-blind men, 12 married, 11 of them having night-blind children, the twelfth had only one child, æt. 2 years at date, and the state of its sight was not known; the other 7 men

* Cases 152, 153, 154, 156, 157, 160.

appear not to have married, or had no issue at date. Of 25 night-blind marriageable females, 18 married, 7 were single; of the 18 who married 12 had some night-blind children, 3 all normal children, and 3 had no issue. In these six pedigrees, therefore, on the other hand, the males transmitted the disease proportionately more often than the females; but the numbers are small and no conclusions are warranted.

I now add the salient facts of every case of this little-known disease that I have been able to find, both from published sources and my own notes. What we want in connection with the subject is a far larger material than has as yet been collected.

Cases.

Group I.—Both Sexes affected; Descent continuous.

Case 151.—The well-known case by Cunier (1838) brought up to date and published fully in 1907 is not only the earliest recorded, but the best example of its kind. For details the reader is referred to the original.* Here we need state only that in nine generations 135 persons were night-blind, that the proportion of females who suffered was slightly larger than the proportion of males, that of the affected persons of each sex who married a larger proportion of the females than of the males had affected children, and that the fundus is perfectly normal in appearance in the 15 living affected members of the genealogy who have been examined.

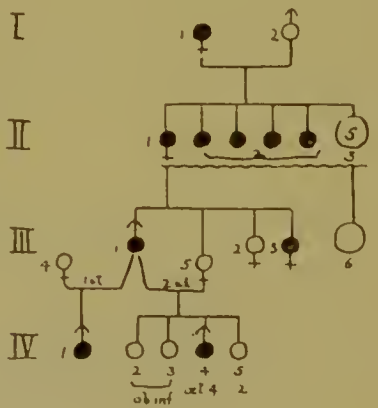
Case and Fig. 152.—Stiévenart's† Case (1847) was almost certainly this disease, not retinitis pigmentosa. Mde. . . . (I, 1), who died æt. 74, had 10 children (II, 1, 2, 3), five of whom were born night-blind and are said to have alternated with normal ones. No case of the disease in descendants of the five normal ones (II, 3). Descendants of four out of the five night-blinds (II, 2) not specified. Fifth (II, 1), lived, like her mother, to be 74, and had three children, of whom first and third (III, 1 and 3) were affected; second (III, 2) normal and nothing recorded

* O.T., vol. xxvii, p. 269 (1907).

† Stiévenart, Note sur une Héméralopie Héréditaire, An. d'Oculist, vol. xviii, p. 163 (1847).

of her descendants. III, 3 married, but had no children. III, 1 married twice, first wife (III, 4) died at first confinement; the child (IV, 1) lived and was night-blind; by second wife (III, 5) had four children, the two eldest (IV, 2 and 3) died of diphtheria at a few days old; third (IV, 4), æt. 4 at date of writing, was night-blind; fourth (IV, 5), aged 2, believed to be normal. The

Fig 152



author saw the four then living affected members (II, 1; III, 1 and 3; IV, 4), and found pupils active to light and eyes o normal appearance; they were rather short-sighted, in daytime saw as well as other people, but could not see at night; the night-blindness was of the same degree in all.

Case and Fig. 153.—Sedan* (1885). ♂, artillery officer, one of Gen. IV, had never been able to guide himself at night; when seen, æt. 30, My. 3·5 D.; colour vision n.; night-blindness not getting worse; no decided contraction of Fs., fundus perfectly normal.

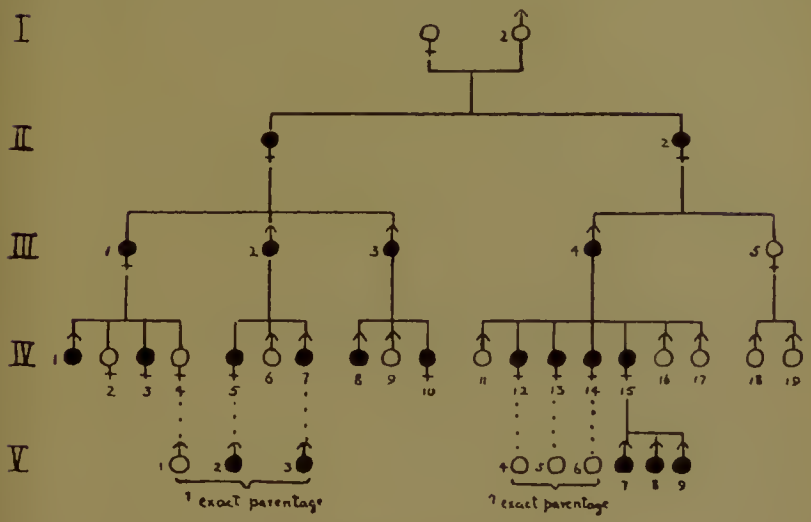
In 1895, Cutler† heard from Dr. Sedan that in Gen. V six new children had been born (V, 1 to 6), of whom two were affected, both males (V, 2 and 3); the exact parentages of these six are not given, nor the sex of 4, 5, and 6. In 1906 I wrote

* Sedan, Rec. d'Ophth., 3rd Ser., vol. vii, p. 675 (1885).

† Cutler, Knapp's Archives of Ophthalmology, vol. xxiv, p. 327.

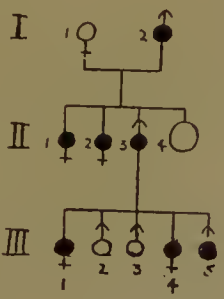
to Dr. Sedan asking further information, but he was unable to supply any, the family having removed.

Fig. 153



Case and Fig. 154.—Atwool* (1895). III, 4, ♀, a hospital nurse, affected as long as she can remember, cannot see to go out alone in the dusk; refraction H., V. 6/6 Sn., 6/12 partly Bjerrum;

Fig. 154



Fs. and colour V. n.; fundus dark but normal; hair dark. III, 5, ♂, clerk; similar symptoms all his life; V. 6/6; Fs. full

* Atwool, these Reports, vol. xiv, p. 260 (1895).

for white and colours in daylight, but much contracted by lowered illumination ; central V., however, not lowered more than that of the (normal) author in diminished light ; colour V. normal, fundus normal. Hair black, irides brown. Father (II, 3), two of his sisters (II, 1 and 2) and their father (I, 2) all similarly affected, the latter (I, 2), a naval officer, is said to have walked overboard in the dark more than once. II, 4 shows several who were not night-blind. I have tried, but failed, to trace this family since the case was published.

Case 155.—Hudson.* ♂, æt. 22, night-blindness well marked as long as he can remember, with My. As. – 1 D. sph. – 2·5 D. cyl. 6 9 ; fundus perfectly normal, F. somewhat contracted. Not getting worse. Eldest brother and their mother have the same complaint, but no other relations that he knows of. Total number of his siblings not stated.

Case and Fig. 156.—Sinclair.† IV, 5, seen æt. 50 (Author's Case II) ; V. 6/5, colour vision normal ; F. for white full in daylight, not reduced by a moderate lowering of light, but in a still lower illumination it became very markedly contracted as compared with F. of a normal person in same light ; Förster's photometer after 20 minutes' adaptation required the opening to be 7 as compared with 2 for a normal ; light-sense therefore = 1/12. Has been night-blind all her life and not getting worse. Fundus perfectly normal.

One of her affected sons seen æt. 11 (probably V, 9) also had V. 6/5, normal colour vision, full F. for white in daylight, and perfectly normal fundus.

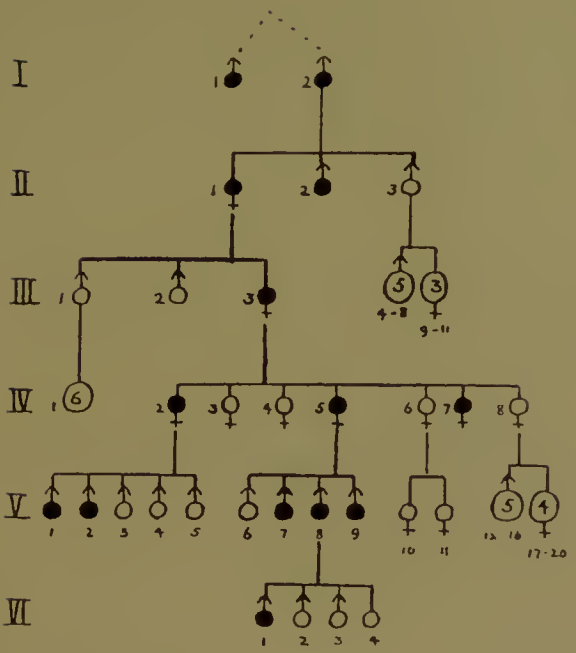
In November, 1907, Mr. Sinclair wrote telling me that the eldest child of V, 8 (VI, 1) is typically affected ; VI, 2, 3, and 4 are still too young for examination. No known consanguinity.

Case and Fig. 157.—(Unpublished) (P. 34, 214, 1895). II, 1, ♂, æt. 51 ; night-blind all his life, not getting worse, gives several striking anecdotes, served in the army and his comrades made allowances for him ; V. 6/9 with and without + 0·5 D. cyl. ; fundus quite normal in both except one or two

* Hudson, The Ophthalmoscope, vol. i, p. 89 (1903).

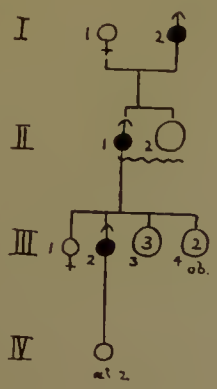
† Sinclair (Walter), Ophthalmic Review, vol. xxiv, p. 255 (1905).

Fig 156



small patches of choroidal atrophy at lower periphery of R. and a good deal of superficial disturbance of choroid at lower periphery of L. No length of stay in the dusk allows his eyes to adapt themselves. No signs of hereditary syphilis. He was the eldest

Fig 157

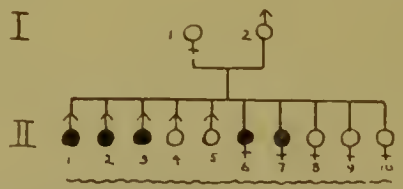


son, number of siblings not given. Father, I, 2, was affected in same way and never went blind. III, 2, second born son of the seven children of II, 1, night-blind; first born, a girl (III, 1), and three other living sibs. (III, 3), normal; two others (III, 4) died. III, 2 has one child, æt. 2 (IV, 1). I have been unable to get more recent information.

Sub-Group of I.—Both Sexes affected, but Descent discontinuous.

Case and Fig. 158.—Swanzy* (1873). Childship of 10, 5 ♂, 5 ♀. Three ♂ and two ♀ night-blind as long as they could remember and were not getting worse. Examined one of

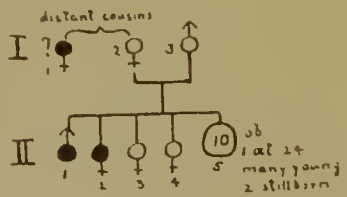
Fig 158



the affected ♂s and both affected ♀s and found fundi n. in all; the ♂s had H. As. and good colour V.; refraction of the ♀s not recorded. Parents not consanguineous and not night-blind. No cases known in earlier generations. In the three examined the night-blindness said not to be so severe in the two sisters as in the brother.

Case and Fig. 159.—Fitzgerald (C.E.)† (1873). Childship

Fig 159



of 14, of whom only four living at date of record, 1 ♂, 3 ♀. Of these four the ♂ and one ♀ (II, 1 and 2) badly night-blind

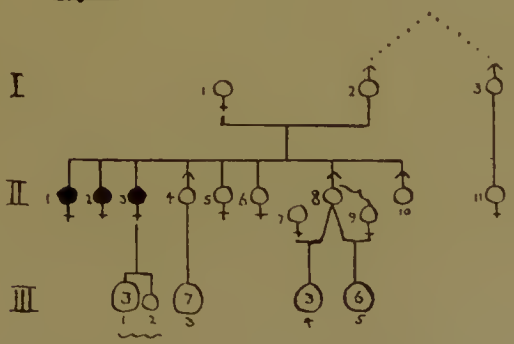
* Swanzy, Irish Hospital Gazette, vol. i, p. 84 (1873).

† Fitzgerald (C. E.), *ibid.*, p. 216 (1873).

as long as they can remember. Only the ♂ (II, 1) examined, aged 35, clergyman, with My. 1/9 (say 4·5 D.), good V., colour V. and F. normal; fundi quite normal. Of the nine siblings not living, two still-born, several died young of "water on the brain" and 1 (♂) at 24, probably tubercle. No consanguinity of parents. A distant cousin of patient's mother said to be night-blind.

Case and Fig. 160.—Cutler* (1895), his Family 2. Three sisters night-blind in childship of eight. II, 3, æt. 37 (Author's case 5), night-blind all her life and not getting worse; V., R. with + 1·5 D. cyl. 5/6, L. – 5·5 D. sph. 5/6 doubtfully; light-sense, after adaptation 1/25; fundus normal in each except that Professor Fuchs found the retinal arteries somewhat too narrow; married 14 years, four children, of whom three living and free from night-blindness, one died at 8 months. II, 3 is one of 8, 3♂, 5♀, all living; two older sisters (II, 1 and 2), æt. 42 and 40, are also night-blind; the other five normal. Two

Fig. 160

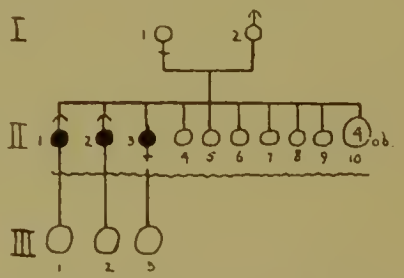


of the sisters in II (which two not mentioned) are married and have respectively nine and three children, all normal (not shown in Figure); two of the brothers (II, 4 and 8) married, one of them twice, his second wife (II, 9) being his cousin; these two brothers had by the three wives, 7, 3, and 6 children, none affected. Blindness from other causes in Generation I, viz.: cataract (I, 1), glaucoma (I, 2), gradual blindness in his brother (I. 3), and his daughter (II, 11), now 15, thought to be blind from birth. Parents of I, 2 and 3 were not consanguineous.

* Cutler (Colman W.), A. f. A., vol. xxx, p. 92 (1895), and A. of O., vol. xxiv, p. 313 (1895).

Case and Fig. 161.—Cutler's Family 3. Night-blindness stationary and dating from birth in three members of a childship of 13. History incomplete. I, 1 and 2, not consanguineous, had 13 children, 4 of whom (II, 10), not night-blind, had died at date of record. Of the 9 living (II, 1 to 9), 3, æt. 44, 42, and 28 (II, 1, 2, 3), are affected with congenital night-blindness;

Fig. 161

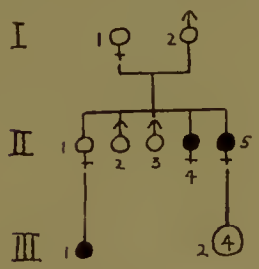


all these three have children (III, 1, 2, 3), and none of them are affected. The only one examined was II, 2, 42 (author's case Heinrich) with V. only 6/18 aided by weak glasses, slight nystagmus, normal central colour-sense, concentric narrowing of Fs. for white; light-sense 1/35; fundus normal. No details as to offspring of the six living unaffected siblings II, 4 to 9.

Professor Fuchs kindly sent me in 1905 the next three unpublished cases, and a fourth, Case 172, in addition to the ones just quoted which were reported from his practice by Cutler.

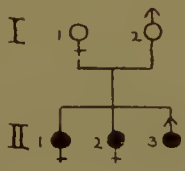
Case and Fig. 162.—Family 1. Rosa Banger, 45 (II, 5), stationary night-blindness; refraction My. 7 to 8 D. V. corrected 6/18; F. for white decidedly contracted; photometer shows very marked lowering of light-perception; fundus normal, except myopic changes and some opacities in vitreous. She is youngest of five and has four children (III, 2) all normal. Her next elder sister (II, 4) night-blind like herself; her three other siblings are normal, but the only child (III, 1), æt. 13, of the eldest (II, 1) is affected. Parents (I, 1 and 2) had good eyes and were not consanguineous.

Fig. 162



[Case and Fig. 163.—Family 2. Benowicz. Three siblings, all night-blind. Parents normal and not consanguineous. II, 1, æt. 15, night-blindness discovered when three years old; V. of each with + 1·5 D. cyl. 6/10 to 6/15; light-sense by Förster's photometer, 1/20; fundus normal. II, 2, æt. 11, night-blindness

Fig. 163

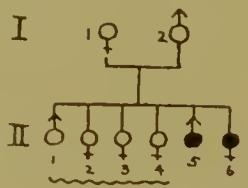


noticed at same age as in 1; V., R. 6/10, L. 6/20; some H. As., but V. not improved; light-sense 1/25; fundus normal. III, 3, æt. 8, night-blind like the others; vision cannot be tested accurately, fundus normal.

Case and Fig. 164.—Family 3. Wenzel. Two siblings affected in six, one myopic, the other not. II. 5, labourer, æt. 22, healthy and all his senses normal except sight; has never been able to go about alone in the dusk; V. – 6 D. 6/18, no As.; F. for white full; light-sense by Förster's photometer 1/12; reads 1 J. easily by daylight, but by diminished light with which the physician reads 1 J. patient can only see No. 5 J.; fundus normal except a considerable myopic staphyloma. Is fifth of six; the youngest (II. 6), æt. 19, night-blind like II, 5,

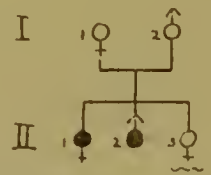
but said not to be short-sighted : the other four normal Parents (I, 1 and 2) healthy eyes and not consanguineous.

Fig 164



Case and Fig. 165.—(Unpublished) (P. 16, 153 ; June, 1888). Two siblings affected. II, 1, æt. 60 ; cannot see at night ; V. 6/18 (H.m. 1·5, corrected) : striæ in lens ; fundi normal except a

Fig 165



small patch of epithelial disturbance at y.s. in L. eye. A brother (II, 2), æt. about 50, has always had bad V. ; blind at night and can only see straight before him. A sister (II, 3) had ocular headaches, but no night-blindness.

Group II.—Only Males affected ; Descent continuous and almost always through the Mother ; Myopia in the Majority of those affected.

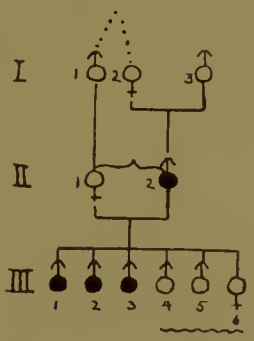
Case and Fig. 166.—Donders* in 1854 described the case of one member of a family, and Maes,† in 1861, supplemented the account ; the following is from the combined sources. In a childship of 6 (III, 1 to 6), 1, 2, and 3 were night-blind with

* Donders, Torpor Retinæ Congenitus Héréditarius. Nederl., Lancet, 1854, May and June. Fully translated into French, An. d'Oculist, vol. xxxiv, p. 270.

† Maes, Over Torpor Retinæ, Inaug. Dissert., Utrecht, 1861, p. 129.

perfectly healthy fundus; Donders saw III, 1 in 1854, aged 16; Maes saw III, 3 in 1860 or 1861, aged 19, with normal V. and refraction. III, 4, 5, and 6 not night-blind. Father (II, 2),

Fig. 166



æt. 58, in 1861, night-blind from "youth" and not getting worse; he and his wife were consanguineous in "sixth degree" (probably second cousins), no cases known in earlier generations.

Case 167.—Förster* (Case 3). ♂, æt. 14, with perfectly normal fundus and V. full in daylight, but even in the daytime could not see in dark rooms or cellars and in the evening had to be led by a guide; in bright moonlight could see pretty well. F. full by daylight and even in the dusk of evening no considerable contraction could be proved. Had been so from birth. A younger brother had the same complaint, but his other siblings (number not stated) and both parents saw as well as other people in the dusk.

Case and Fig. 168.—Maes† saw another family in 1861. In a childship of nine, 3 ♂s and 6 ♀s, the three ♂s (III, 3, 4, 5) were all night-blind from birth. Only one (III, 3) a schoolmaster, examined; My. 1/10 (4 D.); V. corrected was subnormal‡; "Ophthalmoscopic signs of slight atrophy of choroid and retina, but no perceptible changes at y.s." Some of the children of

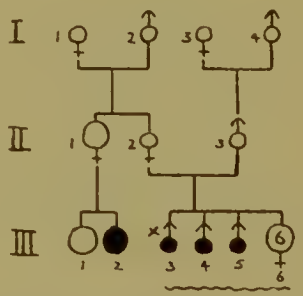
* Förster, Ü. Hemeralopie u. die Anwendung eines Photometers, p. 42 (1857).

† Maes, *loc. cit.*

‡ He is said to have read 1 Jäger with difficulty and very close, and with correction to have seen, in good light, "No. 21 at 6 m."

his mother's sisters similarly affected (III, 2), though these aunts themselves (II, 1) have normal eyes. Patient's parents and grandparents normal eyes and not consanguineous. The records as to refraction, V., and fundus appearances are incomplete,

Fig. 168



but evidently vision was below normal. In the presence of myopia, limitation to males and descent through the mother, the case conforms to the present myopic group.

Case and Fig. 169.—Pflüger,* 1883. Only affecting males. Descent through unaffected females. My. and nystagmus in all the affected. A few other (1 ♀ and 4 ♂) simply myopic without night-blindness.

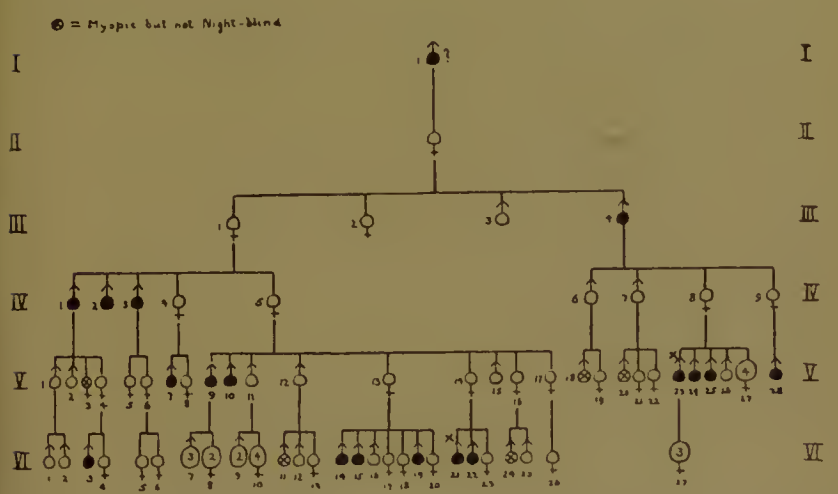
Particulars are given of only two, viz.: V, 23 and either VI, 21 or VI, 22. The former (V, 23), aged 40, at time of record about 1879, had My. 6 D., V. corrected 6/18, convergent strabismus of R.; varying rotatory nystagmus; colour-sense perfectly normal; light-sense much lowered (polariscope test); F. not recorded; fundus quite normal except a crescent down-out equal in size to O.D. The other case (VI, 21 or 22) was seen about 1879, aged 3 years, but the notes could not be found; from memory author states that there was considerable nystagmus, very severe night-blindness, and no decided ophthalmoscopic changes. The pedigree was collected by V, 23, an educated man. The author's general statement is that all the

* Pflüger, Universitäts-Augenklinik in Bern, Bericht ü. das Jahr 1881.

night-blind members were males and had without exception high myopia and nystagmus; five others (1 ♀ and 4 ♂) had simple myopia without other defects. The historical record begins with II, 1 (1751—1821), the night-blindness of her father (I, 1), being only assumed.

Author points out how completely this pedigree agrees with the law formulated by Horner for congenital red-green blindness,

Fig 169



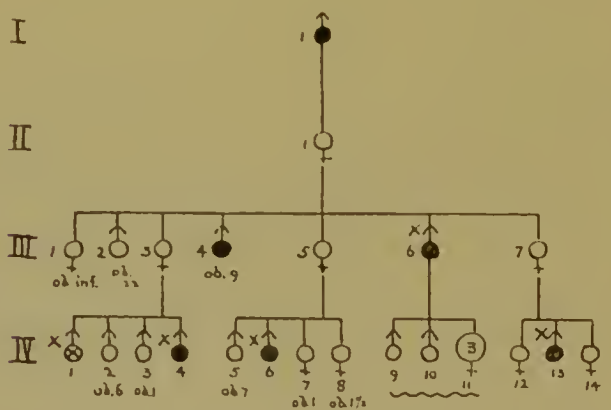
the disease always passing through "a latent stage represented by at least one female generation" but "dying out completely with each male who is not night-blind." Further, that the latency may continue through 2, 3, and even 4 female generations as shown in the ascendants of IV, 1 to 3; V, 7, 9, 10; and VI, 14, 15, etc. Lastly, that "the disease is not weakened by prolonged latency in respect to the number of males attacked" is shown in the children of V, 13. No consanguinity known in any generation.

Case and Fig. 170.—Cutler (his Case I). D.,* a mason (I, 1), lived to be 80, night-blind all his life and did not get worse; always went to bed very early because he saw so badly in the dusk; saw quite well in good light; nothing known of his ancestors. No known consanguinity in entire pedigree. He had only one child,

* Cutler (Coleman W.), *loc. cit.*

♀ (II, 1), who, together with her husband, had normal sight. III, 1 to 7, children of II, 1; of the males, 2 (III, 4 and 6) night-blind; III, 4 died at 9 years old; had been examined by Professor Arlt; III, 6 (Dominic, Author's Case 1), æt. 47 at date, mason, night-blind all his life; L. eye defective, R. 6/12 no As., not improved by glasses, F. for white full; light-sense to Förster's photometer 1/49 (minimum opening 14 mm. compared to 2 mm. for normal person); adaptation for 15 minutes gave slight improvement, but a longer seclusion gave no better result; fundus probably normal; examined by Fuchs twice at interval of three years, and on each occasion lower temporal arteries noted

Fig 170

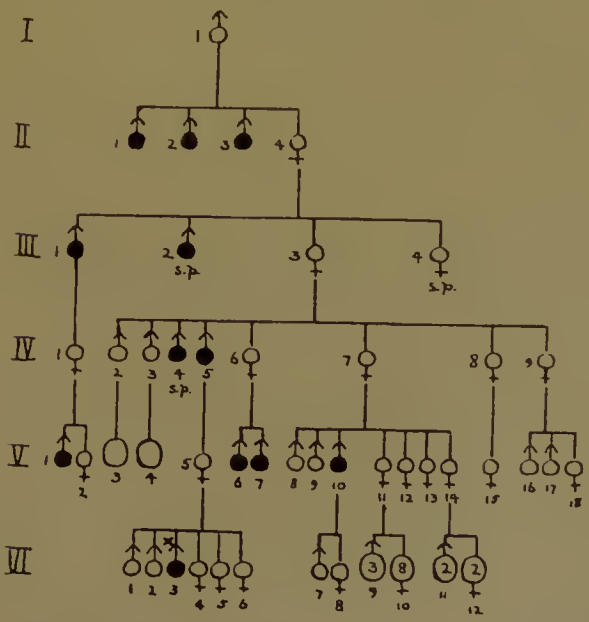


as rather small in comparison with upper ones, which were of full size—no pigmentation or white dots. The other male (III, 2) died at 22; he was not affected, nor were the daughters. Of the latter III, 1 died 14 days after birth; III, 3, a hospital nurse in Vienna in 1895, had four children (IV, 1 to 4), all ♂, of whom the youngest (4), æt. 21 (Author's Case 2), is night-blind; he has 9 D. of My., with V. corrected 6/24 in each eye, 6/18 both together; lateral nystagmus; central colour-sense normal; light-sense after adaptation 1 36; fundus quite normal except a large crescent. IV, 1, æt. 28, also had 9 D. of My., but no night-blindness; light-sense normal (Förster's photometer); V. corrected 6/18; fundus normal except for some spots of choroiditis in various parts. III, 5 has four children, two of

each sex; one of the sons (IV, 6), æt. 13 (Author's Case 4), with My. 2 D., V. corrected 6/18 and normal central colour-vision, suffers from night-blindness, light-sense 1/36 after adaptation, fundus normal except a crescent and oval shape of O.D.; no pigmentation and no white dots. III, 6 has two sons and three daughters, all normal. III, 7 has three children, one of whom (IV, 13), æt. 18, is night-blind (Author's Case 3), slightly H., with V. 6/12 or 6/18; central colour-sense normal; light-sense 1/25 after adaptation; fundus normal except a crescent downwards. IV, 12 and 14, æt. 28 and 17, normal; no record of any conceptions between IV, 12 and 13.

Case and Fig. 171.—Ammann* (1898) Five generations. I, 1 (1750—1838); normal sight; nothing known of his or his

Fig. 171



* Ammann, Das Vererbungsgesetz der Hæmophilie u. d. Nachtblindheit. Correspondenzbl. f. Schweizer Ärzte, 1898, No. 20.

September, 1908.—Since correcting the proof of this case Dr. Ammann has kindly sent me a more extensive pedigree of the family, but only two additional cases of night-blindness have been discovered. II, 1 in Fig. 171 had three daughters and two sons all normal, who would be in III: two of

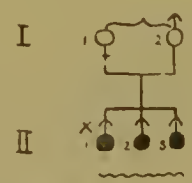
wife's ancestors. Had three sons, all night-blind (II, 1, 2, 3), and one daughter normal (II, 4). Only one of the entire genealogy was examined (VI, 3); he had 9 D. of My., and was night-blind; age not stated; was so bad he could not go about at night. I find no note of ophthalmoscopic examination, but the whole context implies that the fundus was normal. It is stated by VI, 3 that all who were night-blind were also short-sighted, and all who saw well at night had ordinary long sight.

Professor Fuchs sent me the following new case in 1905 :—

Case and Fig. 172.—Family Streitler. Three siblings affected. All males. Myopia in at least one. Consanguinity.

II, 1, ♂, 39, agent; well-marked night-blindness recognised in very early childhood: V. R. −4·5 D., L. −3·5 D., 6/24; slight As.; F. for white full in good light, a little smaller in bad light

Fig 172



(measurements given); fundus normal. Has two brothers (II, 2 and 3) with the same defect, but no note as to their refraction. The notes do not state whether there were more than these three in the childship. Parents (I, 1 and 2) had good eyes; they were distantly related by blood, but exact degree not known.

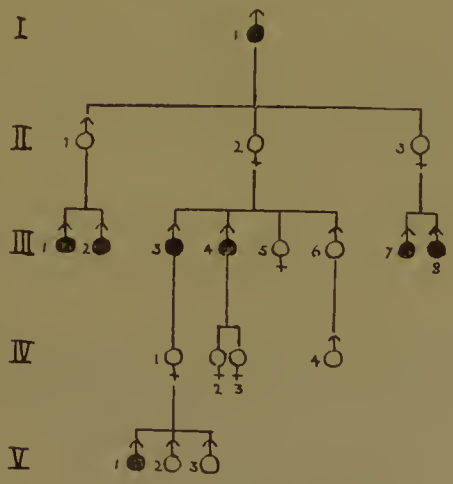
Case and Fig. 173.—Pagenstecher* (1878). Night-blindness without ophthalmoscopic changes affecting males only, in three

the daughters married, one of them had one child only, a night-blind son (in IV) who has left no progeny; the other married daughter had four daughters, all normal, and four sons, of whom three were normal and one night-blind (in IV); this night-blind son has two daughters, both normal, the eldest æt. 20 (in V), and no sons. In the new pedigree II, 3 of Fig. 171 is transferred to Gen. III, and would appear between III, 2 and 3; in other respects Fig. 171 agrees with the new document. The husband of II, 4, his sister, and many of her descendants, have also been traced down to Gen. V, and found to be free from night-blindness.—E. N.

* Pagenstecher (H.), Erblichkeit der Hemeralopie. Hirschberg's Centralbl. f. A., 1878, p. xl (August).

generations; alternate generations, whether male or female, exempt. Myopia in the only adult (III, 3), who was fully examined. I, 1, ♂, Herr J., died 1827. II. Son and two daughters, all normal eyes. III. Seven sons and one daughter of Generation II; six of the sons affected, one (III, 3), Herr M. of the text, had My. of 3 – 4 D.; his age not stated, but as he had a grandson he must have been beyond the age for My. to be progressive. IV. The daughters and one son of middle childship of III all normal. One of them (IV, 1), Frau O. of the text, had three sons (V, 1, 2, 3), of whom the eldest (V, 1) = "P. O." of

Fig. 173



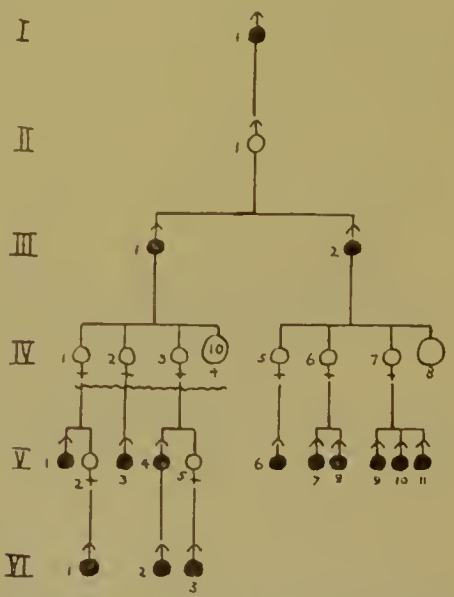
author's text, æt. 4 (1878), was night-blind. The other two were presumably too young at that date for tests to be applied. In 1905 Dr. Pagenstecher had no further information.

Case and Fig. 174.—Stanford Morton.* Males only; My. or My. As. and fair hair in all those affected. Night-blindness does not get worse. Those not night-blind are not short-sighted. Descent through unaffected mother. V, 1. Rev. A. (Author's Case 1), night-blind all his life; V. with My. As. corrected almost normal; colour-vision good; F. much contracted (charts show boundary at 20°, 30°, and 40°, but size of test and

* Morton (Stanford), O. T., vol. xiii, p. 147 (1893); supplemented from my own notes of VI, 1, seen independently (P. 30, 194, 1894).

character of light not stated); fundus quite normal; light hair. VI, 1. Master C. B., 13 (1894), (Author's Case 2 also seen by me at about same period); night-blind like V, 1 and the others; V with My. As. (My. 4 D vertical 2 D. horizontal), corrected, 6/9 partly; colour-vision perfect; Fs. much contracted (smaller than in VI, 1); fundus quite normal. Some of V, 2 to 11, were seen by Mr. Tatham Thompson, of Cardiff; they were night-blind without retinitis pigmentosa, and at least one was

Fig. 174



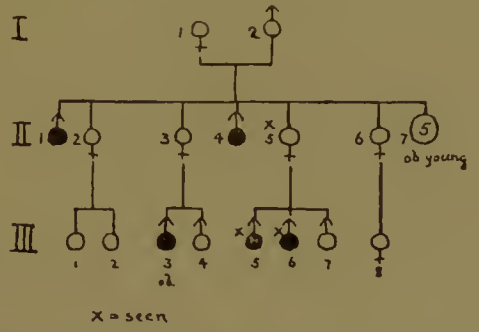
myopic. The only exception to the typical descent is V, 4, an affected ♂, who, if the record is correct, transmitted the disease. It has not been possible to get further particulars of this family.

Case and Fig. 175 (unpublished).—*Night-blindness from infancy or birth limited to males; myopia; descent through females.*

Berner family (St. Thomas's O.P., vol. ii, 163, 1879). I, 1 and 2 not consanguineous; both good sight; 2 was "mad" for some weeks before he died, æt. 77. They had 11 children, as to 5 of whom who died young (II, 7) nothing is known. II, 1 to 6, living. Of these the males (1 and 4) have been night-blind all their lives, not getting worse; the elder (II, 1, æt. 40) wears

glasses in the street (myopia probably); the younger (II, 2, æt. 28) does not. The females, II, 2, 3, 5, 6, all have children (III, 1 to 8); sex of III, 1 and 2, not recorded; of the other six, five ♂ and one ♀, III, 3, was very night-blind and died of diphtheria, æt. 2 years. His brother (III, 4), æt. 7 years at date, saw quite well at night. III, 5, æt. 5, noticed by mother to be night-blind when 12 months old, in other respects quite normal; seen, Ps. n. to light, but rather large; no nystagmus; refraction (under atropine) estimated My. 4 D; moderate crescents, vessels normal; appearance of doubtful coarsening of pigment epithelium

Fig. 175

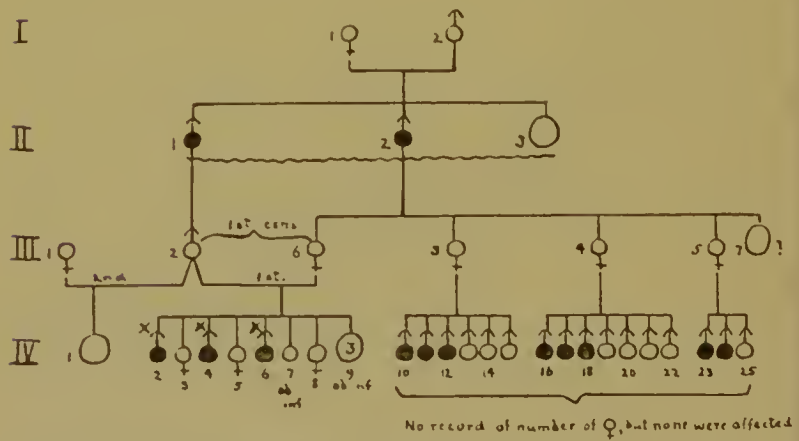


in some parts, but compatible with health; colour vision normal and prompt with wools; dark complexion, gray irides. III, 6, æt. 3, night-blind, refraction under atropine myopic but degree not estimated, small crescents, a single minute dot of black pigment in upper periphery of L.; light hair, blue eyes; ps. often unusually large. Fine lateral nystagmus. III, 7, æt. 12 months, and III, 8, æt. 3 years, said not to be affected. Testimony from II, 5, herself not affected.

Case and Fig. 176 (unpublished).—B. family, not related to the last case (P. 48, 99 (1898) and 56, 14 (1901)). Ages as in 1898 unless stated otherwise. Negative influence of consanguinity. IV, 2, ♂, 40 (43 when seen in 1901), night-blind all his life, not getting worse. For a long time has worn full correction $\left.\begin{matrix} -4{\cdot}5 \text{ sph.} \\ -2{\cdot}5 \text{ cyl.} \end{matrix}\right\}$ and V. with this 6/12; Fs. not taken, seem full in daylight; light-sense (Förster's photometer), 1/16; ps. n. to

light; fundus perfectly normal; v.s. seen fairly with −4 D.; periphery H. about 5 D. IV, 4, ♂, 37, said to be short-sighted and night-blind. IV, 6, ♂, 33, when seen (1898); very night-blind all his life; not getting worse: has worn −5 D. since 19; V. R. $\frac{-6\text{ s.}}{-2\text{ c.}}$ 6/9. L. $\frac{-6\text{ s.}}{-5\text{ c.}}$ 6/24; Fs. not taken; colour vision said to be normal; R. fundus three or four small dots of black in various parts, L. no spots seen; O.Ds. and vessels quite normal in each; no signs of hereditary syphilis. IV, 3, æt. 39, and IV, 5, who died at 24 of "internal cancer," had good sight. IV, 8, 29, exophthalmic goitre, but not night-blind. IV, 7 and

Fig 176

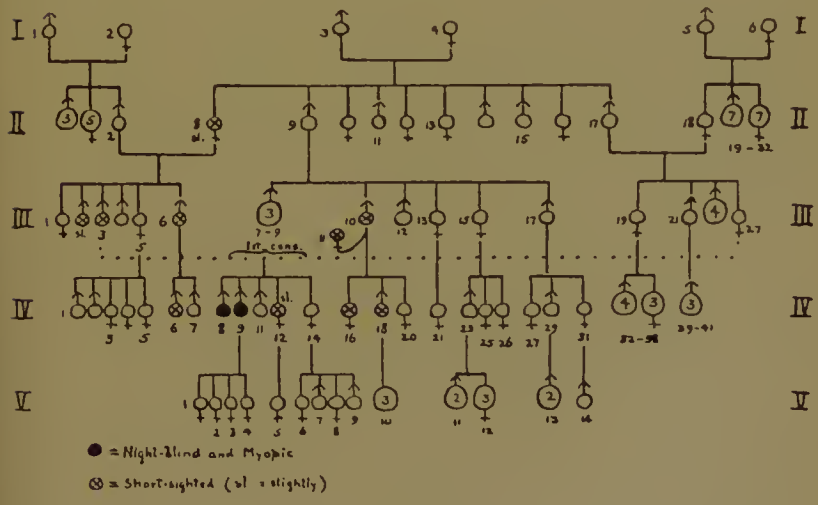


9, four who died in infancy. History chiefly from III, 1, second wife of III, 2, and step-mother of IV, 2 to 9; her account was quite clear and doubtless derived from her husband, III, 2, who was 24 when he married his first wife, II, 6, and was 65 in 1898; in the other groups (IV, 10 to 25) she only gives the history and number of the sons; as no female was affected she omits them from the pedigree. III, 6, first wife and first cousin of III, 2, was the fourth daughter of II, 2; married at æt. 21, of her 10 children six grew up; she died of phthisis at 38. III, 3, 4, 5, the first, second, and third daughters of II, 2; each of them had many sons (IV, 10 to 25), of whom one-half are said (by III, 1) to have been night-blind; no record of

daughters; this information was obtained by letter and not verified by cross-questions. We do not know whether II, 2 had any sons (III, 7). II, 1 and 2, two night-blind brothers; 3, several other siblings, normal. I (1 and 2), normal and not consanguineous.

Case and Fig. 177 (unpublished).—Mr. ——, IV, 9, æt. 47 (1900) (P. 53, 108); night-blind all his life; My., began glasses about æt. 12, and has had −7 D. since he was 25; now My. 9 D. 6/6 Sn.; 6/18 Bjerrum; F. full in daylight, slight concentric contraction in very dull artificial light after 15 minutes' adaptation, and nearly fell over chair in my dark room; photometer after 5 minutes' adaptation shows light-sense 1/50; colour vision very good and quick; teeth good, no signs of

Fig. 177

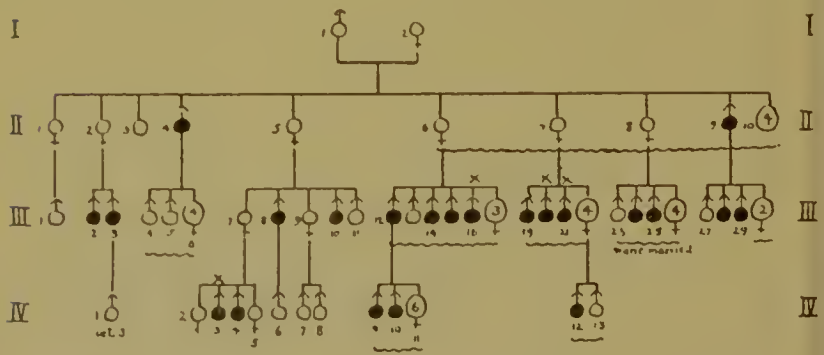


hereditary syphilis; fundi perfectly normal except My. crescents; periphery of fundus, Em. in both. Night-blindness not getting worse. He is second of five. His elder brother (IV, 8) also night-blind. IV, 11, died æt. 39; had very good V., not short, and used to lead the other two at night when they were boys. IV, 12 and 14, ♀ are normal. No other cases in extensive pedigree. In V, none are night-blind, and none at present are myopic, but they are all children. Parents of patient

were first cousins (III, 3 and 27), and the only first cousins who married each other on either side.

Case and Fig. 178.—Howland family.* This was not typical as regards the patient (IV, 3), examined in most detail (Case 20, as previously published), as there were central changes, and also some scattered pigment spots of uncertain significance; yet it would be difficult to place the disease in any other class; the macular changes referred to in this little boy may have been associated with myopia; I saw him three times between the ages of 5 and 10, and neither the My. (1·5 D.) nor the changes

Fig 178



progressed in this interval. It was said that in the entire genealogy, 22 were, or had been, night-blind, all males; 16 of these inherited through the mother; the night-blindness was always discovered in childhood, was said to be very well marked, and remained stationary; all the four affected ones that I examined (III, 16, 20, 21, and IV, 3) were myopic. No consanguinity between the original pair of parents (1, 1 and 2), but the point is not mentioned for any of the later generations.

Single Cases; Records Incomplete.

Case 179.—Thomas† (1873). Single case in a ♂ æt. 12, with normal parents; very night-blind from infancy. Refraction

* These Reports, vol. xi, p. 370, Cases 20—23 (1887).

† Thomas (L.), Rec. de Trav. Soc. Med. d'Indre et Loire (Tours), p. 87 (1872–73).

Em. or H., V. full in daylight; F. full (probably daylight); fundus quite n. Nothing recorded about other sibs., or family history.

Case 180.—Leber* (1877). Woman, æt. 20, congenitally night-blind; F. full in daylight, by dim lamplight defective (indistinct), especially in lower part; My. 1/5 (8 D.) R. V. 20/70, L. V. 20/100; rather large posterior staphyloma, and in L. y.s. region absorption of pigment and a few irregular dark spots; choroidal vessels visible everywhere as red network on dark background, but no other changes. Consanguinity of parents; no other members of the family night-blind.

Case 181.—Vieusse; single case in a ♂, æt. 21, conscript; excused from service after repeated examinations had confirmed his assertion and the statements of his friends, that he had all his life been quite blind at and after sunset; fundus quite normal. Family history not mentioned.

Case 182.—Chibret, 1884. Single case, ♂, seen in 1875, æt. 16, with My. 1/13 V. corrected only 2/5; seen again in 1885, V. and refraction exactly as before. Night-blind from birth; conceals it on account of his work; central V. and Fs. not much diminished by somewhat lowered illumination, but tested in a darkened room cannot see objects that are easily seen by a normal person in same conditions after adaptation. No mention of family history. Lays stress on the amblyopia.

Case 183.—Featherstonhaugh, 1887.—Single case; no history of other cases in the family. ♂, æt. 21, V. R. with $\frac{-\ 75\ \text{s.}}{-\ 25\ \text{c.}}$, 20/40; L. $\frac{-\ 2\ \text{s.}}{-\ 0{\cdot}75\ \text{c.}}$ 20/50; very night-blind from earliest infancy; fundus normal; Fs. for white full in good light; colour vision normal. Very deaf as long as can recollect, membrana tympani normal. In childhood was a somnambulist.

Case 184 (These Reports, xi, 371, 1887; Case XXIV, and later notes, P. 7, 190); single case with myopia.—Seen repeatedly between æt. 11 and 22, and not getting worse; mentally dull, but at æt. 22 was acting as a clerk. R. B., ♂, always blind at night; stumbles over things, and cannot see

* Leber, *loc. cit.*, p. 650.

steps or the kerb at night; once walked into a large heap of snow in the dusk. Short-sighted certainly since æt. 5 or 6; at æt. 9 – 6 D. sph. with – 1 D. cyl. was ordered; at 22, My. 8 D., V. corrected 6/18. Carries his head rotated towards his R. and depressed towards L. shoulder. Colour vision normal; Fs. taken at æt. 11 and 15, somewhat contracted even in daylight. Ophthalmoscope shows extreme difference in refraction at posterior pole (My. 8 D.) and periphery (H. about 1 D.) alike when 15 and 22 years old; no morbid changes, but choroid at periphery looked, on the whole, thinner than at posterior pole; O.Ds. and retinal vessels quite normal. Hearing good. No signs of inherited syphilis. He is an only child; only one other conception (miscarriage).* No consanguinity. No other cases known in the family.

Case 185.—(These Reports, xi, 372. Case XXVI.) ♂, 16 (1886). Night-blind as long as he can remember, and dare not go into unlighted road alone at night; not getting worse. V. unaided 6/18 with each, and not improved by glasses (refraction not noted). Fs. slightly contracted by gaslight. Fundi perfectly normal. Intelligent. Not deaf. No consanguinity. Father for a time quite insane, but recovered.

Case 186.—♂, 68 (P. 21, 119, 1890). Night-blind all his life; could never drive at night for fear of running against milestones. V. failing 18 months, especially for objects above the horizontal (shop-names, etc.); R. slight opacities in lens; fine choroidal changes at y.s. and elsewhere; no retinal pigmentation; V. 6/36. L. more opacity of lens and no change seen at fundus. Æt. 82, Mr. Lawford found R. and L. each 16 J. R. Hm. 1 = 6/12, fundus fairly seen, shows changes suggestive of retinitis circinata. L. fundus cannot be seen. All his sibs. were "short-sighted," but no history of night-blindness in them. The fundus changes in this patient (R. eye) were doubtless senile, and not related to his congenital night-blindness.

Case 187 (unpublished).—(P. 35, 185, 1895.) Single case in ♂, æt. 9, with My., malformation of O.Ds. and remains of

* In my previously published account he is said to have had three sisters. This is incorrect; my notes are quite clear, and the mistake is inexcusable.

pupillary membrane. Now æt. 9, and is using — 3·5 D., ordered when 7½; with this V. = 6/18, O.Ds. reniform in outline, the notch being on the lower outer part of margin, and rather grey in colour; vessels normal; a single dot of pigment at periphery of L.; choroid down and out from O.D. thinner than elsewhere; tag of pupillary membrane on R. iris down and in. F. for white full in daylight; in dull light, still allowing full F. to normal observer, patient's F. reduced 30°—60°; colour vision normal. Night-blindness very marked since æt. 3 years; not getting worse. Good health; born full time; is one of two siblings, the other, ♀, not short-sighted, and sees well at night. Mother said to be "very short-sighted," but not night-blind. No other cases of night-blindness known in family. No consanguinity on either side. In 1902, æt. 16, Mr. Spicer found that with — 4 D. sph. and — 0·5 cyl. he saw 6/12 Sn. and 6/36 to 6/24 Bjerrum.

Case 188 (unpublished).—(P. 37, 92, 1896.) Family history not recorded; ♀, 25½. Night-blindness very definite all her life; friends tell her of it; has to be guided if in strange place. V. each 6/5 partly. Em. Ps. n. to light; Bjerrum 4/9. Slight cortical dotted equatorial cataracts, not hindering view of fundus, which shows no changes whatever. Teeth good. Fs. full in daylight.

Case 189 (unpublished).—(P. 50, 43, 1899.) Single case in second born. Refraction Em. or H.; ♀, 48. Difficulty at night all her life; cannot go alone, and often runs against things; description very graphic. V. 6/5 slight H. Fs. no note; no changes found anywhere in fundi except a single small white dot at outer periphery of L. 1. ♂, died æt. 7 years, "water on brain;" short illness after blow on head by stone; V. was good; was born six years before patient. 2. ♀, patient. 3. ♀, died æt. 19, typhoid. V. was good. Family history not recorded.

Case 190 (unpublished).—(P. 53, 29, 1900.) ♂, 20; H.As.; V. never been good; R. always worse than L.; not getting worse. Night-blind all his life; in dusk cannot find his

way home unless he knows it very well, and cannot drive safely in bad light. Glasses about four or five years. R. chooses about $\begin{matrix} +\ 1\ 5\text{s.} \\ +\ 1\ \text{c.} \end{matrix}$, but H estimated considerably higher. V. has varied at different trials and different observers since 1896 from 6/12 to 6/36. L. with $\begin{matrix} +\ 0{\cdot}5\ \text{s.} \\ +\ 0{\cdot}5\ \text{c.} \end{matrix}$ has varied from 6/9 to 6/24; when V. was worst (R. 6/36 and L. 6/24) there may have been temporary spasm of Acc. Colour vision n.; fundus quite normal. Is 7th of childship of 7; is $3\frac{1}{2}$ years younger than the 6th, and the only one with peculiar sight. Family history not recorded.

N.B.—Any references not given in full in the body of the paper will be found at p. 52.

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